TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

TWENTY-FIFTH SESSION

HELD AT THE NEW WILLARD HOTEL, WASHINGTON, D. C.
MAY 5, 6 AND 7, 1913

EDITED BY
LINNAEUS EDFORD LA FÉTRA, M.D.

VOLUME XXV.

American Medical Association Press
Five Hundred and Thirty-Five North Dearborn Street
CHICAGO

CONTENTS

PRESIDENTS

1889. A. Jacobi, M.D.
1890. J. Lewis Smith, M.D.
1891. T. M. Rotch, M.D.
1892. Wm. Osler, M.D.
1893. A. D. Blackader, M.D.
1894. John M. Keating, M.D.
1895. F. Forchheimer, M.D.
1896. Joseph O'Dwyer, M.D.
1897. Samuel S. Adams, M.D.
1898. L. Emmett Holt, M.D.
1899. Wm. P. Northrup, M.D.
1900. Henry Koplik, M.D.
1901. Wm. D. Booker, M.D.
1902. W. S. Christopher, M.D.
1903. J. P. Crozer Griffith, M.D.
1904. Augustus Caillé, M. D.
1905. C. G. Jennings, M.D.
1906. A. Jacobi, M.D.
1907. B. K. Rachford, M.D.
1908. C. G. Kerley, M.D.
1909. Charles P. Putnam, M.D.
1910. David L. Edsall, M.D.
1911. Henry Dwight Chapin, M.D.
1912. Walter Lester Carr, M.D.
1913. John Lovett Morse, M.D.
1914. Samuel McC. Hamill, M.D.

OFFICERS, 1913

President ..... J. Lovett Morse, M.D.
Vice-President ..... John Ruhräh, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.

COUNCIL

Geo. N. Acker, M.D., *Chairman*

R. G. Freeman, M.D.
Alfred Hand, Jr., M.D.
L. E. La Fétra, M.D.
Isaac A. Abt, M.D.
John Howland, M.D.
Thomas Morgan Rotch, M.D.

MEETING PLACES

1888. Washington, D. C. (Organization), September 18.
1889. Washington and Baltimore, September 20 and 21.
1890. New York, June 3 and 4.
1891. Washington, September 22 and 25.
1892. Boston, May 2, 3 and 4.
1893. West Point, N. Y., May 24, 25 and 26.
1894. Washington, May 29 and June 1.
1895. Virginia Hot Springs, May 27, 28 and 29.
1896. Montreal, May 25, 26 and 27.
1897. Washington, May 4, 5 and 6.
1898. Cincinnati, June 1, 2 and 3.
1899. Deer Park, June 27, 28 and 29.
1900. Washington, May 1, 2 and 3.
1901. Niagara Falls, May 27, 28 and 29.
1902. Boston, May 26, 27 and 28.
1903. Washington, May 12, 13 and 14.
1904. Detroit, May 30, 31 and June 1.
1905. Lake George, N. Y., June 19, 20 and 21.
1906. Atlantic City, N. J., May 30, 31 and June 1.
1907. Washington, May 7, 8 and 9.
1908. Delaware Water Gap, May 25, 26 and 27.

1909. Lenox, Mass., May 27 and 28.
1910. Washington, May 3, 4 and 5.
1911. Lake Mohonk, N. Y., May 31 and June 1 and 2.
1912. Hot Springs, Va., May 29, 30 and 31.
1913. Washington, May 5, 6 and 7.
1914. New London, May 26, 27 and 28.

OFFICERS, 1914

President ..... Samuel McC. Hamill, M.D.
Vice-President ..... Matthias Nicoll, Jr., M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.
Assistant Editor ..... O. M. Schloss, M.D.

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L. E. La Fétra, M.D. — Thomas Morgan Rotch, M.D.
Isaac A. Abt, M.D. — D. M. Cowie, M.D.

MEMBERS

1903. Abt, Isaac A., M.D. ..... 4810 Kenwood Avenue, Chicago
1893. Acker, George N., M.D. ..... 913 Avenue of Presidents, Washington
0 Adams, Samuel S., M.D. ..... 1801 Connecticut Ave., N. W., Washington
1894. Baines, Allen M., M.D. ..... 228 Bloor Street, Toronto
0 Blackader, A. D., M.D. ..... 236 Mountain Street, Montreal
1907. Bovaird, David, Jr., M.D. ..... 137 East Sixtieth Street, New York
1911. Bowditch, Henry I., M.D. ..... 416 Marlborough Street, Boston
1911. Butterworth, William W., M.D. ..... 3914 Prytania Street, New Orleans, La.
0 Caillé Augustus, M.D. ..... 753 Madison Avenue, New York
1911. Carpenter, Howard C., M.D. ..... 1805 Spruce Street, Philadelphia
0 Carr, Walter Lester, M.D. ..... 68 West Fifty-First Street, New York
0 Chapin, Henry Dwight, M.D. ..... 51 West Fifty-First Street, New York
1897. Churchill, F. S., M.D. ..... 1259 North State Street, Chicago
1910. Coit, Henry L., M.D. ..... 277 Mt. Prospect Avenue, Newark, N.J.
1898. Cotton, A. C., M.D. ..... 3218 West Jackson Boulevard, Chicago
1909. Cowie, D. M., M.D. ..... Lawrence Building, Ann Arbor, Mich.
1891. Crandall, Floyd M., M.D. ..... 113 West Ninety-Fifth Street, New York
0 Dorning, John, M.D. ..... 124 West Eighty-First Street, New York
1906. Dunn, Charles Hunter, M.D. ..... 220 Marlborough Street, Boston
1904. Eaton, Percival J., M.D. ..... 131 N. Highland Avenue, E. E., Pittsburgh
1907. Elie, Charles A., M.D. ..... 1927 Chestnut Street, Philadelphia
1895 Freeman, Rowland G., M.D. ..... 211 West Fifty-Seventh Street, New York
1913 Friedlander, Alfred, M.D. ..... 4 West Seventh Street, Cincinnati
1913. Gerstenberger, Henry J., M.D. ..... Ostrora Building, Cleveland
1910. Gittings, J. C., M.D. ..... 3492 Chestnut Street, Philadelphia
1907. Graham, E. E., M.D. ..... 1713 Spruce Street, Philadelphia
1892 Griffith, J. P. Crozer, M.D. ..... 1810 Spruce Street, Philadelphia
1895 Hamill, S. McC., M.D. ..... 1822 Spruce Street, Philadelphia
1902 Hand, Alfred, Jr., M.D. ..... 1724 Pine Street, Philadelphia

1910.	Haynes, Royal S., M.D.	267 West Seventy-Ninth Street, New York
1909.	Heiman, Henry, M.D.	30 West Eighty-Eighth Street, New York
1910.	Herrman, Charles, M.D.	250 West Eighty-Eighth Street, New York
O	Holt, L. Emmett, M.D.	14 West Fifty-Fifth Street, New York
1913.	Hoobler, B. Raymond, M.D.	131 East Sixty-Ninth Street, New York
1905.	Howland, John, M.D.	20 East Eager Street, Baltimore
O	Huber, F., M.D.	209 East Seventeenth Street, New York
O	Jacobi, A., M.D.	19 East Forty-Seventh Street, NewYork
1894.	Jennings, Charles G., M.D.	457 Jefferson Avenue, Detroit
1896.	Kerley, Charles G., M.D.	132 West Eighty-First Street, New York
1905.	Knox, J. H. Mason, M.D.	804 Cathedral Street, Baltimore
O	Koplik, Henry, M.D.	30 East Sixty-Second Street, New York
1903.	Ladd, Maynard, M.D.	270 Clarendon Street, Boston
1903.	La Fétra, Linnæus E., M.D.	113 East Sixty-First Street, New York
1911.	Lucas, William Palmer, M.D.	University California, San Francisco
1912.	McClanahan, H. M., M.D.	468 Brandies Building, Omaha
1909.	Machell, H. T., M.D.	216 St. Clair Avenue, W., Toronto
1907.	Meara, Frank S., M.D.	400 West End Avenue, New York
1898.	Miller, D. J. Milton, M.D.	127 S. Illinois Avenue, Atlantic City, N. J.
1896.	Morse, J. Lovett, M.D.	70 Bay State Road, Boston
1908.	Nicoll, Matthias, M.D.	124 East Sixtieth Street, New York
O	Northrup, William P., M.D.	57 East Seventy-Ninth Street, New York
1910.	Pisek, Godfrey R., M.D.	36 East Sixty-Second Street, New York
1912.	Porter, R. Langley, M.D.	240 Stockton Street, San Francisco
O	Putnam, Charles P., M.D.	63 Marlborough Street, Boston
1891.	Rachford, B. K., M.D.	323 Broadway, Cincinnati
O	Rotch, Thomas Morgan, M.D.	197 Commonwealth Avenue, Boston
1905.	Ruhräh, John, M.D.	839 North Eutaw Street, Baltimore
1900.	Saunders, E. W., M.D.	3003 Lafayette Avenue, St. Louis, Mo.
1912.	Schloss, Oscar M., M.D.	172 West Seventy-Ninth Street, New York
1913.	Sedgwick, Julius P., M.D.	2015 Kenwood Parkway, Minneapolis
1902.	Shaw, Henry L. K., M.D.	361 State Street, Albany
1891.	Snow, Irving M., M.D.	476 Franklin Street, Buffalo
1905.	Southworth, Thomas S., M.D.	807 Madison Avenue, New York
1911.	Talbot, Fritz B., M.D.	311 Beacon Street, Boston
1910.	Tileston, Wilder, M.D.	424 Temple Street, New Haven
1912.	Veeder, Borden S., M.D.	1806 Locust Street, St. Louis, Mo.
1895.	Wentworth, A. H., M.D.	352 Marlborough Street, Boston
1896.	Westcott, Thompson S., M.D.	1720 Pine Street, Philadelphia
1913.	Wilcox, Herbert B., M.D.	159 East Seventieth Street, New York
1897.	Williams, Harold, M.D.	528 Beacon Street, Boston
O	Winters, J. E., M.D.	25 West Thirty-Seventh Street, New York

Note.—The first column gives the date of election to the Society. The organizers of the Society are designated by "O," the date being 1888.

HONORARY MEMBERS

Dr. John Thompson	Edinburgh, Scotland
Dr. George F. Still	London, England
Dr. O. Heubner	Berlin, Germany
Dr. William Osler	Oxford, England
Dr. A. Baginsky	Berlin, Germany
Dr. V. Hutinel	Paris, France
Dr. Charles Rauchfuss	St. Petersburg, Russia

Deceased

John A. Jeffries, M.D.
Born, September 2, 1859,
Died, March 26, 1892.

Thomas F. Sherman, M.D.
Born, March 17, 1856,
Died, September 26, 1893.

John M. Keating, M.D.
Born, April 20, 1852,
Died, November 17, 1893.

Charles Warrington Earle, M.D.
Born, 1845,
Died, November 19, 1893.

J. Lewis Smith, M.D.
Born, October 15, 1827,
Died, June 9, 1897.

Joseph O'Dwyer, M.D.
Born, October 12, 1841,
Died, January 7, 1898.

John Henry Fruitnight, M.D.
Born, November 9, 1851,
Died, December 18, 1900.

Frederick A. Packard, M.D.
Born, November 17, 1862,
Died, November 1, 1902.

Walter S. Christopher, M.D.
Born, 1859,
Died, March 2, 1905.

Leroy Milton Yale, M.D.
Born, February 12, 1841,
Died, September 12, 1906.

James Park West, M.D.
Born, June 27, 1858,
Died, June 25, 1908.

Frederick Forchheimer, M.D.
Born, 1853,
Died, June 1, 1913.

CONSTITUTION AND BY-LAWS OF THE AMERICAN PEDIATRIC SOCIETY

ARTICLE I

Name and Object of the Society

The Society shall be know as the American Pediatric Society, and shall hold an annual meeting.

It has for its object the advancement of the knowledge of physiology, pathology and therapeutics of infancy and childhood.

ARTICLE II

Proceedings

The proceedings shall consist of:

1. Discussions on subjects previously selected.
2. Original communications.
3. Demonstrations of gross and microscopic preparations, apparatus, and instruments.

ARTICLE III

Members

The Society shall be composed of two classes of members to be designated: (1) active members and (2) honorary members.

The number of active members shall be limited to seventy-five.

The number of honorary members shall be limited to twenty-five.

ARTICLE IV

Election of Active Members

Nominations to membership, signed by two members of the Society, must be made in writing at least one meeting prior to election.

Nominations should be made to the Secretary, whose duty it shall be to require the nominators to write a personal letter endorsing and stating the qualifications of the nominee, and at the same time furnishing a list of the nominee's professional position and publications, with reprints of the latter, when obtainable.

It shall be the duty of the Secretary to transmit to the chairman of the council all the above papers pertaining to each nominee, at least three months prior to his possible election.*

* In the event that required information relating to candidates for membership is not furnished to the Secretary by three months before the time of the meeting at which they would be considered, such candidates for election shall be held over for another year. (Resolution adopted 1912.)

The chairman of the council shall transmit the above-named papers to the other members of the council in the order of their seniority as council members, the junior member of the council returning them to the Secretary.

It shall also be the duty of the Secretary to furnish a printed list of all nominees at least once a year to every member of the Society, and it shall be the duty of the members of the Society, without solicitation, to furnish the council with any information that they may possess as to the fitness of the nominees to become members of the Society.

On nomination by the council, members shall be elected by the Society by ballot. A two-thirds vote of the members present shall be necessary for election.

ARTICLE V

Election of Honorary Members

Physicians of sufficient eminence to merit the distinction may be elected honorary members, to a number not exceeding twenty-five. Such members shall be entitled to attend all meetings and take part in the proceedings, but cannot vote. Honorary members shall be elected in the same way as active members.

ARTICLE VI

Initiation Fee and Annual Dues

Election to membership shall be completed by the payment of an initiation fee of $10.

Each active member shall pay an annual fee, the amount of which shall be decided at each annual meeting.

Honorary members shall be exempt from fees.

ARTICLE VII

Officers

The officers shall consist of a President, Vice-President, Secretary, Recorder [and Editor], Treasurer and a delegate to the Congress of Physicians and Surgeons.

The officers shall be elected annually on nomination by the council.

ARTICLE VIII

Duties of Officers

The duties of the President, Vice-President, Secretary and Treasurer shall be those usual to these offices. The Recorder [and Editor] shall secure the papers read and see that proper notes are taken of the discussions thereon for the use of the committee on publication.

ARTICLE IX

The Council

The council shall consist of seven members, the senior member being chairman. One member of the council shall be elected each year. Four members shall constitute a quorum. The senior member shall retire at the end of each year and shall not be immediately eligible to reelection.

ARTICLE X

Duties of Council

The duties of the council shall be to consider nominations for membership and report them to the Society. The votes of four members of the council shall be required for nomination. The council shall also nominate the officers of the Society and shall decide the time and place of meeting.

ARTICLE XI

Committee of Arrangements

The President, Secretary and the chairman of the council shall constitute a committee of arrangements, the President being chairman of this committee. They shall arrange the details of the meeting and the preparation of the program, and they shall have the authority to invite guests to attend the meeting and to participate in the discussion.

ARTICLE XII

Publication Committee

The Secretary, Treasurer and Recorder shall constitute a committee on publication, to which shall be referred all papers, reports and other matters intended for publication.

All papers presented shall become the property of the Society.

ARTICLE XIII

Amendment of Constitution and By-Laws

Proposals for amendments of the constitution and by-laws must have been made at the meeting previous to that at which they are voted on, the notice for which shall contain an announcement of the proposed changes. Such changes shall require, for their adoption, an affirmative vote of three-fourths of the active members present.

ARTICLE XIV

Termination of Membership

A member may be expelled from the Society for conduct unbecoming a physician and a gentleman. In such cases, formal charges must be made in writing by two members, which shall be referred to the council.

Membership shall lapse for any one of the following reasons:

(1) Absence from three consecutive meetings without excuse acceptable to the council; (2) failure to present and read a paper for five consecutive years; the Secretary in both these cases shall notify members one year before date of possible lapse; (3) non-payment of dues for two years, two notifications having been sent by the Treasurer.

ARTICLE XV

Quorum

Any number of members present at the appointed time of the annual meeting, shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for the expulsion of members, or for altering the constitution and by-laws, twenty-five members shall be necessary.

ARTICLE XVI

Order of Business

1. The President shall call the meeting to order and deliver an annual address. In his absence the Vice-President shall preside, and in the absence of all these officers, the chairman of the council.

2. When a general discussion is arranged by the council, the two members appointed to open the discussion shall not occupy more than twenty minutes each; subsequent speakers shall be restricted to ten minutes each.

3. Papers shall not exceed twenty minutes in the reading. In the discussion following the reading of such papers, remarks shall be limited to ten minutes. Should any paper be too long to be read in twenty minutes, the writer must prepare an abstract which can be read within that time.*

4. At the business session the report of the council as a committee on nominations to office and to membership, shall be made, and ballot shall be held thereon.

Adopted May 28, 1909

* In order to expedite the publication of the Transactions all members whose papers are to appear in the volume, be required either to have their articles in the hands of the editor before July 1 or to have them in process of publication in some medical journal by that date. In the latter event, the editor of the Transactions is to be notified what journal will publish the paper and reprints or galley proofs are to be furnished to him as soon as possible. (Resolution adopted 1912.)

MINUTES OF THE TWENTY-FIFTH ANNUAL MEETING OF THE AMERICAN PEDIATRIC SOCIETY

Held at the New Willard Hotel, Washington, D. C., May 5, 6, 7, 1913

The meeting was called to order at 10:30 a. m., by the President, Dr. John Lovett Moore, of Boston. The following members were present: Drs. George N. Acker, Washington; Samuel S. Adams, Washington; Allen M. Baines, Toronto; A. D. Blackader, Montreal; Henry I. Bowditch, Boston; Walter Lester Carr, New York; Henry Dwight Chapin, New York; F. S. Churchill, Chicago; Henry L. Coit, Newark; D. M. Cowie, Ann Arbor; John Dorning, New York; F. Forchheimer, Cincinnati; Rowland G. Freeman, New York; J. C. Gittings, Philadelphia; E. E. Graham, Philadelphia; J. P. Crozer Griffith, Philadelphia; S. McC. Hamill, Philadelphia; Alfred Hand, Jr., Philadelphia; Royal S. Haynes, New York; Henry Heiman, New York; Charles Herrman, New York; L. Emmett Holt, New York; John Howland; A. Jacobi, New York; Charles G. Jennings, Detroit; Linnaeus E. La Fétra, New York; William Palmer Lucas, Boston; H. M. McClanahan, Omaha; H. T. Machell, Toronto; John Lovett Morse, Boston; William P. Northrup, New York; Godfrey R. Pisek, New York; R. Langley Porter, San Francisco; B. K. Rachford, Cincinnati; Thomas Morgan Rotch, Boston; John Ruhräh, Baltimore; Oscar M. Schloss, New York; Irving M. Snow, Buffalo; Thomas S. Southworth, New York; Fritz B. Talbot, Boston; Borden S. Veeder, St. Louis; A. H. Wentworth, Boston; J. E. Winters, New York.

There were introduced as guests: Drs. James B. Atlee, Chattanooga; John B. Manning, Seattle; William Weston, Columbia; J. D. Love, Jacksonville; Alan Brown, Toronto; R. D. Moffatt, New York; Philip Van Ingen, New York; Herbert B. Wilcox, New York; L. R. De Buys, New Orleans; J. H. M. A. Von Tiling, Poughkeepsie; C. H. Johnston, Grand Rapids; Hubert M. Rich, Detroit; C. S. Dodding, Ann Arbor; Frank Leech, Washington; Copeland, Washington; Ong, Washington; Louise Taylor-Jones, Washington; Hess, Washington; Harvey Wiley, Washington.

The minutes of the twenty-fourth annual meeting were adopted as published in the Transactions of the Society.

The following papers were read:

1. The President's Address by Dr. John Lovett Morse: "Whooping-Cough: A Plea for More Efficient Public Regulations Relative to the Control of This Most Serious and Fatal Disease."

2. Dr. Rowland G. Freeman: "The Diagnosis and Treatment of Pyelitis in Infancy."

The paper was discussed by Drs. Carr, Southworth, Bowditch, and closed by Dr. Freeman.

3. Dr. Langley Porter: "Cases of Pancreatic Insufficiency in Children."

4. Drs. David Murray Cowie and W. S. Hubbard: "A New and Rapid Method for the Estimation of Total Fats in Infants' Stools."

5. Drs. Mathias Nicoll, Jr., and H. L. Wilcox: "Is Diphtheria Frequently a Bacteremia?"

6. Dr. Thomas S. Southworth: "The Ammoniacal Diaper and Its Correction."

The paper was discussed by Dr. Cowie and the discussion was closed by Dr. Southworth.

7. Dr. L. Emmett Holt: "Duodenal Ulcers in Infancy."

The paper was discussed by Drs. Churchill, Griffith, Pisek, Graham, McClanahan and Nicoll. The discussion was closed by Dr. Holt.

8. Dr. Henry I. Bowditch: "Casein in Infant-Feeding—Experiments in Exact Percentages."

9. Dr. Maynard Ladd: "The Influence of Casein on Gastric Motility in Infants."

The papers of Dr. Bowditch and Dr. Ladd were discussed by Drs. Graham, Pisek, Churchill and Griffith, and the discussion was closed by Dr. Bowditch and Dr. Ladd.

At this point in the proceedings Dr. Adams presented a case for diagnosis.

The symptoms and physical signs presented were discussed by Drs. Weston, South Carolina; De Buys, New Orleans; W. P. Northrup, New York, and J. D. Love, Jacksonville. The discussion was closed by Dr. Adams.

10. Dr. Charles Herrman: "Acute Infectious Jaundice in Children."

The paper was discussed by Dr. Forchheimer.

11. Dr. Henry T. Machell: "A Case of Hirschsprung's Disease with Operation and Recovery."

The paper was discussed by Drs. Graham and Griffith, and the discussion closed by Dr. Machell.

12. Dr. J. C. Gittings: "The Relation of the Physician to Social Service."

The paper was discussed by Drs. Talbot, Churchill and Gittings.

13. Dr. Henry Heiman: "A Case of Bilateral Hydro-Ureter-Chronic Pyocyaneus Infection."

The paper was discussed by Dr. Love of Jacksonville, and the discussion was closed by Dr. Heiman.

14. Dr. Henry D. Chapin: "Cases of Edema in Infants."

The paper was discussed by Drs. Hand, La Fétra, Nicoll, Blackader, McClanahan and Machell, and the discussion was closed by Dr. Chapin.

15. Dr. Walter Lester Carr: "Demonstration of a Modified Mackenzie Ink Polygraph."

16. Dr. Thomas Morgan Rotch: "Three Types of Occlusion of the Esophagus in Early Life."

The paper was discussed by Dr. Griffith.

17. Dr. William P. Northrup: "Needle in the Left Ventricle of the Heart (Roentgen-ray)."

18. Drs. Godfrey R. Pisek and L. T. LeWald: "Further Studies of the Anatomy and Physiology of the Infant Stomach, Based on Serial Roentgenograms."

The paper was discussed by Drs. Ladd, Chapin, Talbot, Cowie, Heiman, Blackader, and closed by Dr. Pisek.

19. Dr. Irving M. Snow: "A Case of Intussusception in Which the Diagnosis was made with the Roentgen Ray."

The paper was discussed by Dr. Southworth and Dr. Snow.

20. Dr. H. M. McClanahan: "Why Does the Operation for the Removal of Adenoids Frequently Fail to Relieve Mouth Breathing?"

The paper was discussed by Drs. Heiman, Chapin, Carr, Holt, and the discussion was closed by Dr. McClanahan.

21. Dr. Alfred Hand, Jr.: "Report of a Case of Rabies."

The paper was discussed by Dr. Nicoll.

22. Dr. George N. Acker: "Parotitis Complicated with Meningitis."

The paper was discussed by Drs. Holt, Nicoll and Acker.

23. Dr. Samuel S. Adams: "Cerebellum, Tumor of (Case)."

The paper was discussed by Drs. Lucas and Adams.

24. Dr. John Howland: "The Retention of Calcium by Infants and the Factors Influencing This."

The paper was discussed by Drs. Talbot, Holt and Howland.

25. Drs. J. H. Mason Knox and Martha Tracy: "Phosphorus Excretion in the Urine of Artificially Fed Infants."

26. Dr. Fritz B. Talbot, in conjunction with Drs. Dodd, Foote and Peterson: "Experimental Scorbutus and the Roentgen-Ray Diagnosis of Scorbutus."

The paper was discussed by Drs. Wentworth, Heiman, Howland, Northrup, and the discussion was closed by Dr. Talbot.

27. Dr. William Palmer Lucas: "Therapeutic Measures in Cardiac Cases."

The paper was discussed by Dr. Gittings.

28. Dr. Charles Hunter Dunn: "Cardiac Diseases in Childhood, with Special Reference to Diagnosis."

The paper was discussed by Dr. Harvey S. Wiley (guest), and by Drs. Northrup, La Fétra, Heiman and McClanahan. Dr. Dunn closed the discussion.

29. Dr. David Murray Cowie: "Studies on the Incubation Period."

30. Dr. A. D. Blackader: Mucous Cyst of the Cecum in a Child of Ten Weeks, Producing Occlusion of the Ileocecal Valves, and Simulating a Case of Intussusception. Resection of Gut. Death on the Sixth Day.

The following papers were read by title:

1. "Acid Intoxication in Children," by Dr. Isaac A. Abt.

2. "Amebic Dysentery in Infancy and Early Childhood," by Dr. W. W. Butterworth.

3. "Some Unusual Cases of Cyclic Auto-Intoxication (Cyclic Vomiting)," and "The Use of the Stomach Tube before and after, and Without Operation, in Pyloric Stenosis of the New Born," by Dr. E. W. Saunders.

4. "Pneumococcus Meningitis and Meningismus" and "Acute Lymphatic Leukemia (Three Cases)," by Dr. Francis Huber.

5. "Angioneurotic Edema, Urticaria and Purpura in a Nursing Baby," by Dr. Irving M. Snow.

6. "Pneumonia; Pyelocystitis; Otitis Media; Mastoid Disease. Fever for Eight Months in an Infant Aged 6 to 14 Months. Failure of Vaccines and Apparent Cure with Roentgen Ray (Case)," by Dr. D. J. Milton Miller.

EXECUTIVE SESSION, MAY 7, AT 10 A. M.

The report of the Council was read by the chairman, Dr. George N. Acker.

Excuses for absence had been received from Drs. Eaton and Abt.

The Council recommended as officers for the ensuing year for President, Dr. Samuel McChesney Hamill; Vice-President, Dr. Matthias Nicoll, Jr.; Secretary, Dr. Samuel S. Adams; Recorder and Editor, Dr. L. E. La Fétra, with the appointment of Dr. O. M. Schloss as assistant for one year; Member of the Council, Dr. D. M. Cowie.

As the place of meeting for 1914, the Council recommended New London, Conn., and the date of meeting May 26, 27, 28, 1914.

As a delegate to the Fourth International Congress of the School of Hygiene, the Council recommended Dr. J. H. Mason Knox.

It was recommended that the expenses for the preparation of the index for the Transactions, amounting to about $390, be paid.

The Council recommended for election to membership in the Society Dr. Julius Parker Sedgwick, Minneapolis; Dr. B. Raymond Hoobler, New York; Dr. Herbert B. Wilcox, New York; Dr. Henry John Gerstenberger, Cleveland; Dr. Alfred Friedlander, Cincinnati.

That the assessment of $10 be made for the annual dues.

That the Transactions of the Society be printed by the American Medical Association.

The recommendations of the Council were adopted unanimously by the Society.

The following resolution was introduced by Dr. Nicoll:

"*Resolved*, That until such time as it has been established by recognized medical authorities that inoculation with a secret bacterial preparation is without ill effects, this Society is strongly opposed to its employment, as a preventive measure, in infants and young children."

After discussion of the resolution by Drs. Freeman, Pisek and Adams, the resolution was unanimously adopted by the Society.

SAMUEL S. ADAMS, *Secretary.*
L. E. LA FÉTRA, *Recorder.*

WHOOPING-COUGH

A PLEA FOR MORE EFFICIENT PUBLIC REGULATIONS RELATIVE TO THE CONTROL OF THIS MOST SERIOUS AND FATAL DISEASE

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PRESIDENT'S ADDRESS

According to the mortality statistics compiled by the United States Census Bureau in 1906, from a registration area comprising slightly less than one-half of the population of the United States, there were 6,324 deaths from whooping-cough in that area in children under 5 years of age. The United States *Public Health Reports* show that in 1910 the death-rate per hundred thousand was as follows: whooping-cough, 11.4 per cent.; scarlet fever, 11.6 per cent.; measles, 12.3 per cent., and diphtheria, 21.4 per cent.

In order to get some more recent statistics, I wrote to all the state boards of health, asking for the number of deaths from whooping-cough, scarlet fever and diphtheria during the year 1911, and also for those from bronchitis and bronchopneumonia in children under 5 years of age. I also asked for information as to the state regulations regarding notification, quarantine, disinfection and school attendance in relation to whooping-cough. The reports from thirty states show that 6,251 died of whooping-cough, 1,232 from scarlet fever and 9,579 from diphtheria in these states during the year 1911. Three thousand eight hundred and sixty children under 5 years of age died of bronchitis and bronchopneumonia during the same period in eleven states in which 1,216 died of whooping-cough. It is, of course, impossible to know in how many of these cases the bronchitis and bronchopneumonia were secondary to whooping-cough. They were undoubtedly due to it, however, in a considerable proportion of them. These deaths should be added to those from whooping-cough. The relative mortality from whooping-cough, scarlet fever and diphtheria is essentially the same throughout the country, whooping-cough being almost everywhere more fatal than scarlet fever and less fatal than diphtheria. Whooping-cough is an especially serious disease in the Southern states, as is shown by the fact

that in North Carolina 736 children died of whooping-cough in 1911 against a total of 447 from scarlet fever, measles and diphtheria combined. The death-rate from whooping-cough in North Carolina in 1911 was 32.2 per cent. against 11.4 per cent. for the whole United States.

I also wrote to the boards of health of a considerable number of cities scattered all over the United States, asking the same questions, and received replies from sixty-one, ranging in size from Livingston, Mont., with a population of 5,000, to New York (Manhattan and Bronx), with a population of 2,760,000. If Chicago and New York are excluded, the relative mortality from the three diseases under consideration is the same as that in the United States as a whole. When they are included, the figures are as follows: whooping-cough, 1,327; scarlet fever, 2,014; diphtheria, 3,539.

There were 6,908 deaths from bronchitis and bronchopneumonia in children under 5 years of age in forty cities in which there were 1,022 deaths from whooping-cough. Although there were many exceptions, the death-rate from whooping-cough was, on the whole, as would be expected, greater in the large cities than in the small.

It hardly seems necessary to give any more statistics to prove what a serious and fatal disease whooping-cough is and to show that, instead of being a trifling affair as it is usually considered to be by the laity, it is a condition of the utmost gravity. "Any disease which kills ten thousand children per annum is," as Rucker says, "a serious one. If bubonic plague were to kill that many children in the United States in one year, the whole world would quarantine against our country. A child dead of whooping-cough is just as dead as a child dead of plague." Certain other points in relation to the mortality are, however, of great importance.

German statistics, covering a period of eleven years, show that the mortality among those attacked with the disease is: Under 1 year of age, 26.8 per cent.; between 1 and 2 years, 13.8 per cent.; between 2 and 5 years, 3 per cent., and between 5 and 15 years, 1.8 per cent.

Ninety-six per cent. of the 6,324 deaths from whooping-cough in the United States in 1906 were in children under 5 years of age. Fifty-seven per cent. of the fatalities were in the first year, 23 per cent. in the second, 8 per cent. in the third, 4 per cent. in the fourth and 2.5 per cent. in the fifth year. It is a comparatively mild affection in healthy children over 5 years old, and after puberty it is rarely fatal. The

importance of these figures will be evident when the measures to be taken to control the disease are considered.

What is being done in this country to limit the spread and diminish the death rate from this dread disease? Surprisingly little. It is a notifiable disease in only twenty-nine of the forty-three states that answered my inquiry on this point. The health officers of many of these states say, moreover, that very little attention is paid by physicians to the law requiring notification. Isolation is required by law in seven states and "modified" isolation in two others. It is recommended in another, but the secretary of the board of health states that it is rarely enforced. "Some attempt is made at it" in another, while in another authority is given to the counties to isolate it, but the secretary of the board of health states that few counties take advantage of this authority. The disease is placarded in six states, perhaps in more. Thirty-one states do not require isolation.

Disinfection after the disease is required by law in four states and "recommended but rarely enforced" in one. "Some attempt is made at it" in another, and in another authority is given to the counties to disinfect, of which authority they do not take advantage. "Modified" disinfection is required in two states. No disinfection is required in thirty-four. The impression obtained from the letters is, however, that both isolation and disinfection are chiefly on paper and that they amount to little or nothing practically.

Two states, at least, have no law forbidding the attendance of children ill with whooping-cough at school. The others forbid attendance at school, but only three of the states from which I received answers have any regulations as to how long they shall be kept out of school. The other children in the family are not allowed to attend school in seven states. They are allowed to attend school in eleven, whether they have had the disease or not; in six, if they have had it, and in two if the patient is isolated. There is no state regulation as to the attendance of the other children in the family in nine states. I was unable to get definite answers from the others.

The regulations of the cities, both large and small, average better than those of the states. Notification is required in forty-four of the sixty-one cities from which I received replies, but isolation is demanded in but twenty. Judging from the letters, however, the isolation is in many cases very imperfect. Some other cities placard, but do not

isolate. Disinfection is required in but five, while it is "advised" in two others.

Strange as it may seem, children with the disease are allowed to go to school in three of the sixty-one cities, two of these cities being in Ohio and one in Mississippi. The other children in the family are allowed to attend school in twenty-seven. They are not allowed to attend school, unless they have had the disease, in ten; unless they have had the disease and live away from home, in two; or until after three weeks from the last exposure, in two. In the others they are not allowed to attend school under any conditions.

There is almost no provision for the hospital treatment of whooping-cough in this country. In New York there is a special ward for children with whooping-cough at Bellevue, but only those having complications are admitted. There are also two isolation cottages, each containing fifteen beds, for whooping-cough at Randall's Island. Six hundred and eight cases were treated there from 1903 to 1912, inclusive, with nineteen deaths, all of them from complications. These wards are not open, but in fair weather the children are kept out of doors as much as possible. There are no special hospitals or hospital wards for the treatment of whooping-cough in Chicago, although cases with complications are sometimes admitted to the contagious department of the Cook County Hospital and there isolated. The Philadelphia General Hospital has a separate section for children with whooping-cough. Boston has no provision for these cases. They are admitted to the isolation hospital in San Francisco, but only the most serious, complicated cases are taken and there is no special whooping-cough pavilion. There is a ward of eight beds devoted entirely to whooping-cough at the Charity Hospital in New Orleans. One pavilion in the new Cincinnati General Hospital is to be arranged exclusively for whooping-cough and at the Johns Hopkins Hospital cases are to be admitted and treated in small isolating rooms. Several of the hospitals in the smaller cities occasionally admit cases of whooping-cough with severe complications to their contagious hospitals and treat them in separate rooms. Most of the general hospitals throughout the country refuse whooping-cough entirely, although some of them at times take severe, complicated cases and treat them in separate rooms. If children with the disease are admitted by mistake, they are sent home, unless so ill that this is not possible, when they are isolated in separate rooms. These, as far as I can find out, are the only provisions made in the United States for the treatment of this disease.

which at one time or another affects almost every member of the community and which causes 10,000 or more deaths yearly!

There is no general rule as to the management of children with whooping-cough in outpatient and dispensary clinics. In most clinics the children at their first visit mix freely with the other children in the waiting-room until they are discovered by the physician. In a few, the children are seen by a physician before they go to the waiting-room and many of the cases are then discovered. In the majority of the clinics the children are not allowed to return for treatment, but are referred to district or dispensary physicians. In others they are allowed to return and are "treated on the sidewalk" at the beginning or end of the clinic, or are admitted to separate rooms where they are at once treated and sent home. Judging from what I have seen of outpatient clinics in my own and other cities, the isolation obtained in this way must be very incomplete and very unsatisfactory. In some clinics no attempt whatever is made to separate these patients from the other children in the waiting-room and they are allowed to return as often as they wish. It is hard to imagine any better method for disseminating the disease. In two or three clinics, however, they are treated at an entirely different hour from the other patients.

The precautions taken in other countries to prevent the spread of this disease are but little, if at all, better than those in this country. It is not a notifiable disease in England or Scotland and there is no quarantine or disinfection after it in either country. Children with the disease are not allowed to attend school, the time limit in England being six weeks. The other children are not allowed to attend school, unless they have had the disease and do not attend the lower grades or after a quarantine of twenty-one days. Children with whooping-cough are admitted to the "fever hospitals." Five hundred and seventy cases were treated in the Metropolitan Asylums Board hospitals in 1911, the first year in which this disease was admitted, with a mortality of 12.1 per cent. There is a special ward of eight beds for whooping-cough at the Great Ormond Street Hospital and a special suite of rooms for it at St. Bartholomew's. There is a special clinic for whooping-cough in special rooms, twice a week, at a special time of day, at the Great Ormond Street Hospital, and a special clinic in the afternoon at the Victoria Hospital for Children.

Whooping-cough is a notifiable disease in Austria, but there is practically no quarantine or disinfection. Neither the patients nor other children in the family are allowed to attend school. It is admitted to special wards in some hospitals and to the infectious hospitals, and is treated in special rooms in the outpatient departments. It is not a notifiable disease in Bavaria and there is no quarantine or disinfection after it. The patient is not allowed to attend school. There are no special hospitals and the precautions taken in the outpatient departments are rudimentary. Czerny in Strasburg treats children with whooping-cough in the open wards. It is a notifiable disease in Graz, but there is no quarantine and no disinfection after it. That is, the customs are as varied as they are in this country.

Notification of whooping-cough is voluntary in France. Isolation and disinfection depend on notification. The children are not allowed to return to school until thirty days after the disappearance of the paroxysms. The regulations as to the other children depend on the locality. Children with whooping-cough are admitted to the hospitals and treated in special rooms or in small wards in isolation pavilions. The precautions taken in the outpatient departments are very rudimentary. It is evident, therefore, that the neglect to take proper precautions to prevent the spread of this disease and to provide hospital accommodations for its care is not confined to this country, but is wellnigh universal.

It is self-evident that more should be done to limit the spread of whooping-cough than is now being done and that more strenuous efforts should be made to diminish the terrible mortality from this disease than are now being made. In order to take intelligent measures to limit its spread, it is necessary, however, to know first the nature of the contagion and when and how it is transmitted.

The recent investigations of Mallory have proved conclusively that the Bordet-Gengou bacillus is the cause of whooping-cough and that the organism is present between the cilia of the epithelium lining the trachea and bronchi. This organism is present in the sputum in the catarrhal stage and is most abundant at this time and in the first two or three weeks of the spasmodic stage. It has been found in the sputum as late as the eighth week of the spasmodic stage. It is fair to assume, therefore, that the disease is transmitted by the secretions of the respiratory tract and that, while most contagious during the catarrhal and early weeks of the spasmodic stage, it is also contagious throughout the whole

of the spasmodic stage. Kittens, puppies and monkeys may be infected with the disease. This probably happens so seldom under ordinary conditions, however, that infection from animals can, for practical purposes, be disregarded. The Bordet-Gengou bacillus is very easily destroyed outside of the body. Indirect contagion is, therefore, very unusual and of but little importance. The staining of smears of the sputum by proper methods gives reasonably satisfactory results. The isolation and recognition of the organism by cultures is, however, too complicated a procedure for practical every-day use. An agglutination reaction is present in many cases, but is not constant and is usually not very high. Its presence is proof of whooping-cough; its absence does not count much against it. A complement-fixation reaction is present in a considerable proportion of children with whooping-cough and convalescent from it. The frequency of the reaction increases with the duration of the disease. Both of these tests are, however, too difficult of performance to be of practical utility for every-day use. The complement-fixation reaction should be of great service in the recognition of abortive and atypical cases in exceptional circumstances, when such recognition is of great importance.

There is an increase in the total number of white corpuscles with an absolute and relative increase in the number of lymphocytes in the catarrhal stage of whooping-cough. The leukocytosis and lymphocytosis increase with the severity of the disease, reaching their highest point in the paroxysmal stage. There is either no leukocytosis or a leukocytosis with a relative increase in the polynuclear neutrophils in the diseases with which whooping-cough may be confused. This blood-formula is a fairly constant one in whooping-cough and is therefore of considerable assistance in its diagnosis before the appearance of the characteristic whoop. It is, however, not always present and may be absent, if there is some complication which is accompanied by a polynuclear leukocytosis. Due allowance must also be made in infants and young children for the normally high percentage of lymphocytes at this age. While the examination of the blood and sputum will unquestionably be of assistance in limiting the spread of whooping-cough by rendering it possible to recognize it in its early stages and thus to isolate children with it earlier than would otherwise be done, it does not solve the problem, because until the health authorities, physicians and public appreciate the importance and gravity of the disease, such examinations will not be made often enough to make any appreciable difference. In the future,

when these facts are recognized, they will undoubtedly be of great assistance.

In the immediate future and probably for many years to come, it is reasonable to suppose that, because of the indefiniteness of the early symptoms and the frequency of mild types of the disease, almost every one will sooner or later have whooping-cough. This fact, while unfortunate and presumably eventually remediable, is not so serious as it at first sight appears, when it is remembered that about 95 per cent. of the deaths from whooping-cough occur during the first five years and the great majority of these in the first two years. The most important thing, then, is to keep babies and young children from having the disease.

The first step to be taken is to convince physicians and the public in general of the seriousness of whooping-cough in infants and young children and of the importance of protecting them from it. All regulations, no matter how well planned, will be useless until those interested in enforcement are so convinced. They can be convinced only by a campaign of education. This campaign will have to be led by the pediatrists and the United States public health authorities, since they are the only ones who at present seem to appreciate the importance of the subject. When the public and physicians are properly educated, regulation will be relatively simple.

Whooping-cough must be made everywhere a reportable disease and the same penalties imposed for failure to report it as in the case of smallpox, scarlet fever and diphtheria. The house should be placarded and the inmates instructed by the health authorities as to the seriousness of the disease in infancy and the methods to be employed to prevent contagion. The sputum and vomitus should be treated in the same way as in tuberculosis.

The patients should be separated from the other children in the family, if they are under 5 years of age. If such separation is impossible, the patients should be removed by the health authorities to special hospitals provided for the purpose. These hospitals should be constructed on the "shack" plan in order to give the children the maximum amount of fresh air and thus to prevent the development of complications and cross-infection, and so situated that the children can be up and out of doors in suitable weather. There is no reason why children should be isolated in one room and not allowed to go out of doors, provided they are kept away from other children. They ought not to be

allowed on the street, but, in order to protect other children in case they do get on the street, they should be required to wear an arm-band of some prescribed color and labeled "whooping-cough" in large letters. They should not be allowed under any circumstances to visit places of public congregation or to travel in public conveyances. Children who fail to observe the quarantine regulations should at once be sent to the hospital by the public authorities, no matter what their circumstances or social position. They should not be released from quarantine until after the cessation of the paroxysmal cough or until at least six weeks have elapsed since the onset, even if the paroxysmal cough has ceased. It is to be hoped that in the future quarantine will be maintained until after the cessation of the paroxysmal cough and the disappearance of the Bordet-Gengou bacillus from the sputum.

The vitality of the Bordet-Gengou bacillus outside of the body being slight, formal disinfection is not necessary. Thorough cleaning and airing of the premises is all that is required.

The other children in the family should not be allowed to attend school unless they have already had the disease or until two weeks have elapsed since the last exposure, provided they are free from catarrhal symptoms. It is possible that this period of two weeks may be too short, the evidence as to the length of the incubation period of whooping-cough being unsatisfactory. Present observations seem to show, however, that it varies between two and ten days. Two weeks should, therefore, be amply sufficient.

Children with catarrhal symptoms, in whom there is any reason to suspect the possibility of whooping-cough, should be excluded from school. It is probable that in the future the examination of the sputum will be used as a test in the same way that the bacteriologic examination of the throat is now used when diphtheria is suspected.

The community should be required to establish hospitals not only to take care of those children that cannot be or are not properly isolated at home, but also to take care of those babies and children ill with the disease that cannot be properly treated in their homes.

It can be confidently predicted that when the physicians and the public understand what whooping-cough really means, when proper regulations for its control are established and enforced and when sufficient hospital accommodations for its care are provided, whooping-cough will cease to be the scourge which it now is.

70 Bay State Road.

THE DIAGNOSIS AND TREATMENT OF PYELITIS IN INFANCY

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The pyelitis of infancy, which is a fairly common disease, is generally understood by pediatricians, as expressed in their writings, as a disease characterized by an active, remitting temperature, and which is treated most successfully by the use of alkalies, while some cases may be cured oy hexamethylenamin in doses of ½ to 2 grains three times a day, or every three hours.

Recent experiences have led me to believe that such statements should be materially modified. We should rather say that the pyelitis of infancy is a disease which is usually characterized by a high remitting temperature, but may give rise to no temperature, and that while some patients may be cured safely by neutralization of the urine with alkalies and others by doses of hexamethylenamin such as those named, that the most efficient treatment in difficult cases is by the use of very large doses of hexamethylenamin aided by vaccines, either commercial or autogenous. In confirmation of this statement I wish to present briefly three cases of pyelitis which I have recently had under observation.

CASE REPORTS

CASE 1.—A healthy female child, 1 year old. One month after a vaccination, which took well, and when it was practically healed the child suddenly had a temperature of 104 F. and examination of the urine showed a pyelitis. Alkaline treatment was prescribed and in four days the urine had cleared and the child had a normal temperature. Nine days later, however, the temperature again arose and the alkaline treatment was prescribed, but after three days, the temperature having gradually risen to 105.6 F., the alkaline treatment was stopped and hexamethylenamin was given in doses of 1 grain every four hours. (Chart 1.) This was changed two days later to 1 grain every three hours and again in two days to 1 grain every two hours, and finally to 1 grain every hour, without any evident effect on the symptoms. The hexamethylenamin was then stopped, it being considered unsafe to continue this dose for many days. Potassium citrate in doses of 5 grains every three hours was again ordered and it neutralized the urine, but under this treatment the temperature began to rise again. At this time a blood examination showed 22,000 white corpuscles, 56 per cent. polynuclears, 3,800,000 red cells and no malarial organisms. The urine drawn by a

catheter showed colon bacilli as well as a few colonies of streptococci. Thirty millions of commercial colon vaccines were then administered. Administration of the vaccine was followed in two days by a normal temperature, which, however, quickly reacted up, on the fourth day having reached nearly 102 F., so that on the fifth day a second dose of 50,000,000 colon vaccines was administered, followed immediately by a normal temperature.

The child was then put on benzoate sodium with hexamethylenamin, 12 grains of each during the day. The following day this was increased to 15 grains and the day after to 24 grains. On this day, however, the temperature again arose to 101.5 F. On the twentieth day of the disease the child's weight was 21¼ pounds, showing a gain of 2¼ pounds during the preceding four weeks. The child began to gain weight as soon as the temperature was reduced by the vaccines. The following day, the temperature having risen to 101.4 F., 40,000,000 bacteria were again administered with a prompt reduction in the temperature. The urine continued to show many leukocytes and bacteria. Twenty-four grains

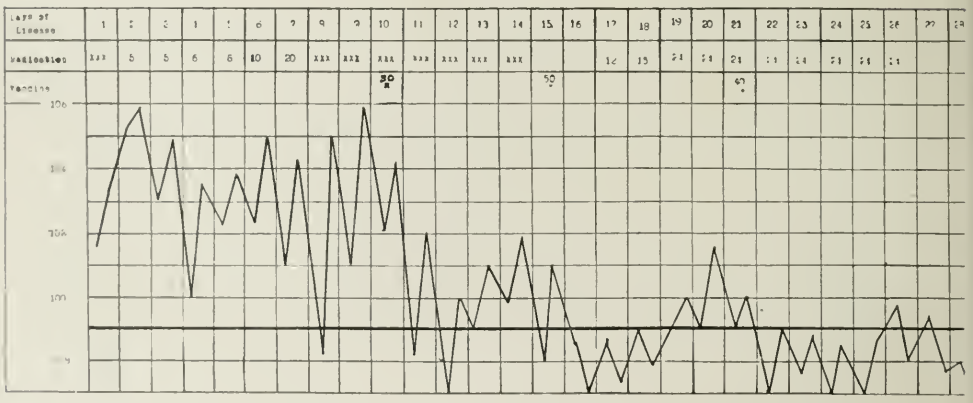


Chart 1.—(Case 1) Temperature curve in an infant with pyelitis. X = millions of vaccine.

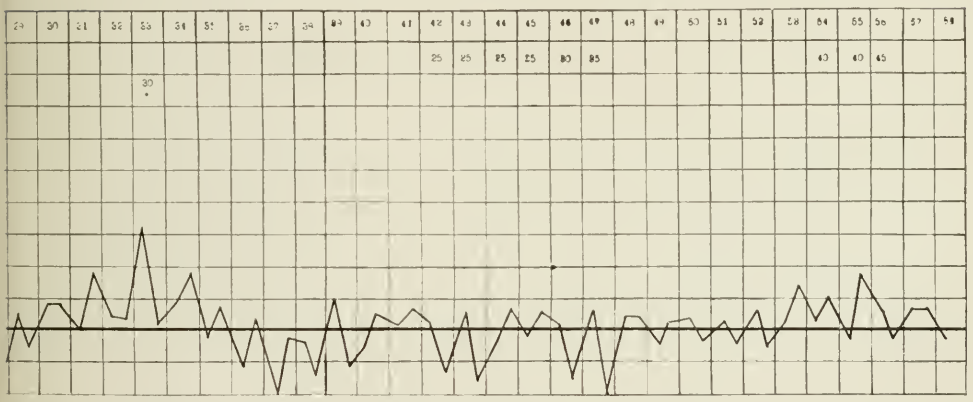
of hexamethylenamin daily was continued until the twenty-seventh day of the disease when the following report on the urine was received from Dr. F. C. Wood: "The only Gram-negative bacillus which was found was not the colon, as it did not ferment sugar. There were ordinary staphylococci in small numbers. The specific gravity was 1.010. It showed no albumin or diacetic acid, but many leukocytes and bacteria."

All medication was now stopped. Six days later, the temperature having again arisen to 102.2 F., 30,000,000 of the same vaccines were administered. No further medication was attempted until the forty-second day when it was decided to try the effect of very large doses of hexamethylenamin for short periods. Twenty-five grains daily without sodium benzoate were then given for four days with a marked diminution in the number of leukocytes and bacteria present. On the fifth day this was run up to 30 grains and on the sixth day to 35 grains, with still a diminution in the bacteria and leukocytes, but without obtaining a sterile urine and without any evidence of irritation of the kidneys. There was no albumin in the urine, and no diacetic acid. On the fifty-

fourth day of the disease, after a week without treatment, 40 grains of hexamethylenamin were administered with an improvement in the urinary condition, and on the following day 40 grains and the third day 45 grains, at which time the urine was found to be sterile. Treatment was then stopped and no recurrence of the urinary infection has occurred during the year that has passed.

These large doses of hexamethylenamin neither caused any evidence of disturbance of the kidneys nor any interference in the well-being of the child. As soon as the fever was controlled by the vaccines the child gained in weight and really seemed better when on large doses of hexamethylenamin than at any other time.

CASE 2.—It is interesting to note the long period of lack of fever and constitutional symptoms, but with a continuation of the pyelitis as evidenced by



Arabic numerals = grains of hexamethylenamin. Roman numerals = grains of citrate of potash.

pus and bacteria in the urine after the administration of vaccines, especially in connection with the next case of which I wish to speak in which a similar infection of the urinary tract with colon bacilli occurred in a child 9 months old, who seemed apparently well at the time the urinary infection was found. This child had been under my care since birth and had never had a febrile disturbance.

Dec. 21, 1912, I found that the urine of this apparently healthy child was moderately acid, had a specific gravity of 1.015, contained a faint trace of albumin, a moderate amount of acetone, a faint trace of phenol, clumps of pus and many bacteria, some in chains. The child was put on potassium citrate, 5 grains every three hours. A specimen taken by catheter showed a pure culture of colon bacilli.

After five days of this alkaline treatment, there being no improvement in the condition of the urine, ½ grain of hexamethylenamin was ordered to be given every three hours, so that the child got three grains that day, on the twenty-seventh 5 grains, on the twenty-eighth 10 grains, on the twenty-ninth 12 grains, on the thirtieth 15 grains, and 18 grains on the thirty-first. During this time

the urine continued to contain leukocytes and bacteria, the leukocytes varying in number from 12 to 50 in a D field. On January 1, 20 grains of hexamethylenamin were administered, on the second 25 grains, and on the third 30 grains. This dose was continued until the sixth of January, when the urine still continued to be contaminated. The hexamethylenamin was stopped and potassium citrate was again administered. The contamination of the urine continued under this treatment, although several times the urine appeared almost free from contamination, and on this account the alkaline treatment was continued longer than it otherwise would have been. On January 27 four doses of 7 grain each, or 28 grains of hexamethylenamin were given, and on the twenty-eighth 35 grains, on the twenty-ninth 35 grains. On the thirtieth macules appeared on the body, especially adjacent to the upper part of the diaper, and the child had a temperature of 101 F. the night before. She was not taking her bottles very well and had lost ½ pound in four days and the hexamethylenamin was stopped.

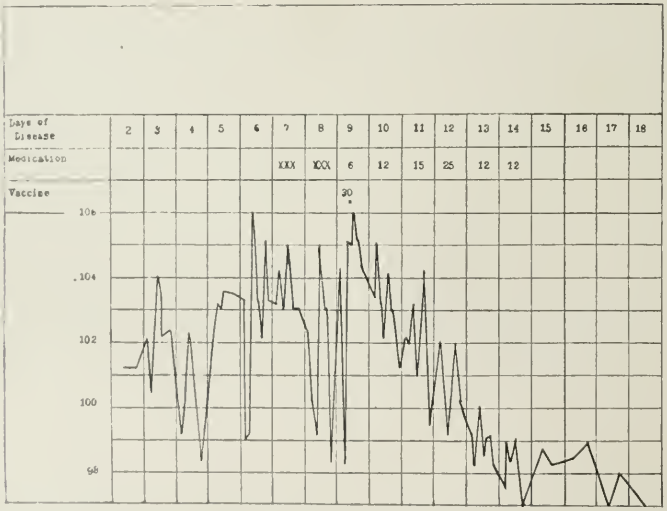


Chart 2.—(Case 3) Temperature curve in an infant with pyelitis. X = millions of vaccine. Arabic numerals = grains of hexamethylenamin. Roman numerals = grains of citrate of potash.

With these large doses of hexamethylenamin the urine rapidly cleared and the day after it was stopped a specimen of urine was found to be sterile and no contamination of the urine has since occurred.

This case, then, of colon pyelitis without temperature in an 18-pound baby was cured by 35 grains of hexamethylenamin a day for three days without any evidence of irritation of the kidney or marked interference of the general health. Whether the macules on the body, the loss of half a pound in weight, and the slight rise in temperature were due to the hexamethylenamin I am unable to say.

No vaccines were used in this case as vaccines appear to control the constitutional symptoms and to have little or no control over the inflammation.

CASE 3.—A third case was recently seen by me in consultation with Dr. Thomas F. Lancer. A female child, 6 months old, had been sick six days. On the day preceding the one when I saw the child the temperature had reached 106 (Chart 2). There was a pause at the end of inspiration and an expiratory grunt, and the movements from the bowels contained some mucus.

By a system of exclusion a probable diagnosis of pyelitis was made, and the child was put on potassium citrate. An examination of the urine showed a colon pyelitis. After three days on potassium citrate, although the temperature had been lower, the child looked much worse and the temperature arose again to 106 F. Thirty million colon bacilli were then administered and 6 grains of hexamethylenamin were given on this day. No immediate marked decline in temperature followed the administration of vaccines. The following day 12 grains of hexamethylenamin were given, on the eleventh day 15 grains, on the twelfth day 25 grains, and on the thirteenth day the temperature was normal and the urine was sterile.

No disturbance of the child's health was caused by the large doses of hexamethylenamin, 25 grains a day in a 6-months' baby. The urine never contained more than a faint trace of albumin.

CONCLUSIONS

Pyelitis in infancy, due to the invasion of the pelvis of the kidney with colon bacteria resulting in a purulent inflammation, can apparently occur with no perceptible rise of temperature at any time. These cases should be treated and cured by the means ordinarily used in pyelitis.

The alkaline treatment of pyelitis, while it is safe and will control many cases, is markedly less efficient than other methods of treatment.

Vaccines, either autogenous or commercial, are useful in controlling the constitutional symptoms of pyelitis.

Hexamethylenamin, while sometimes effective in doses of from ½ to 2 grains several times a day, will not in these doses cure certain cases which may be controlled by very large doses.

Hexamethylenamin should always be administered in small doses first, but the dose should be rapidly run up, the child and its urine being carefully watched for symptoms of irritation of the kidneys.

Large doses of hexamethylenamin should not usually be continued for more than a week at a time, and then after several days without any treatment or with alkaline treatment it should be started at the maximum dose given before and the amount increased daily until an influence on the urine is obtained. Doses of 25 grains daily in a child of 6 months, and from 35 to 45 grains a day in a child from 9 to 12 months may be safely given in this way to some infants.

211 West Fifty-seventh Street.

DISCUSSION

DR. CARR: In some cases we find that urotropin in small doses causes kidney irritation, but if it is discontinued for a short time and then begun again it can be gradually run up into larger doses, even though the first doses irritated the kidneys. Last week I saw in consultation a child 6 years of age, in which the treatment was not started early. The urine showed the presence of colon bacilli. A high intestinal irrigation was given and the temperature dropped. If vaccines had been given, the drop in temperature would have been attributed to the vaccines. The rises in temperature in this case were intermittent.

DR. SOUTHWORTH: I am glad that Dr. Freeman brought out the fact that some of the cases of pyelitis run without temperature. I have been brought into touch with one of these cases which had a definite amount of pus in the urine, but no rise in temperature. It occurred here in the city of Washington during extremely warm weather and I saw it in the North afterwards. There are, however, cases that run continuously high temperatures as well as cases that run remittent temperatures. In the administration of citrate of potash it is possible to have a nascent salt by employing the Liquor Potassii Citratis of the pharmacopeia, which is almost universally made up freshly, whereas the crystals of citrate of potash kept in the drug stores deteriorate by exposure to the air.

DR. BOWDITCH: I would like to ask Dr. Freeman as to whether he tested the urine for reaction during the course of treatment with urotropin. In Dr. Talbot's work on the subject, the authors concluded that urotropin and hexamethylenamin acts only when it is broken up in the form of formaldehyd. This they found happens only in acid urine and to a very slight degree, if any, in alkaline urine. I would like him to tell us of his experience in that line during this course of treatment of this case. I think his treatment is extremely interesting and I am surprised to see how high he went in giving urotropin. The treatment of this disease by culture is, I think, also interesting, especially the small increase in doses and the periodicity of the treatments. I think we are all much indebted to Dr. Freeman for this very interesting paper.

DR. FREEMAN: I wish to emphasize the possible danger of the use of such large doses of urotropin as shown in these cases, for I once saw a child of eight months cyanotic after a ½ grain dose, the cyanosis recurring a second time on the administration of the same amount. So that in the treatment of these cases a small dose of urotropin should be used first and the child and the urine should be carefully watched daily during its administration. I wish also to emphasize the fact that the vaccines which gave such good results were commercial and not autogenous vaccines, for it has been asserted that only autogenous vaccines are useful in pyelitis.

PANCREATIC INSUFFICIENCY *

LANGLEY PORTER, M.D.
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A severe indigestion of acute onset and protracted course, characterized by the evacuation of bulky, pale-gray, greasy stools, occurs fairly often in early childhood. Marked wasting is a feature, as is the occurrence of periods of amelioration during the earlier months of the affection. The stools invariably contain a large amount of wasted fat which is excreted unsplit, and in the graver examples of the disease starches are passed undigested, and sometimes proteins even escape digestive action.

English writers have called this symptom group "Coeliac disease." Robert Hutchison has written a lucid clinical description of it, and in his paper he quotes opinions of Cheadle, Gee and Gibbons on the subject. Eustace Smith has also considered this symptom-complex at length in his lectures on "The Wasting Diseases of Children." The English writers seem inclined to attribute the fat waste to an unexplained diminution in the fat-absorbing powers of the celiac lymphatic system.

In America, Herter, searching for a type of possible onset for those cases of infantilism which he believed to be of intestinal origin, made a study of such cases which he describes as acute and subacute intestinal affections leading to infantilism. His account is worthy of reproduction:

HERTER'S INFANTILISM

Such cases begin, for the most part, between the end of the first and the middle of the third year; they are characterized by diarrhea, usually without tenesmus, with an abundance of mucus but no blood. The diarrheal discharges are usually not frequent, while the loss of weight is not rapid — about one-half ounce daily — it may progress until the child is much emaciated. There is usually considerable flatulence. There is a moderate or marked fall in hemoglobin; the temperature is normal, or subnormal, the appetite is unimpaired. The disease lasts from three to six weeks and recurrences are very apt to occur. The carbohydrates are very badly tolerated and many relapses are certainly due to their incautious use. The urine gives intense reaction to indican and to aromatic oxyacids. Examination of the Gram-stained fields from the stool of a typical example of this infection shows it to consist almost wholly of Gram-positive bacilli, presenting the morphological characteristics of the simple form

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of *Bacillus bifidus*. This organism can be readily cultivated; the *Bacillus infantilis* is obtainable from some, perhaps all, of the stools, and from the intestinal mucus it grows freely, sometimes almost alone when planted in fermentation tubes.

He further states that the very small number of Gram-negative bacteria to be seen in these fields is very striking. Herter's description of Gram-positive bacteria in the stools in such cases was corroborated by Panton in two of Hutchison's series. Apparently Herter would consider the cases explained by enteritis due to invasion by unusual bacterial forms.

French authors, Carnot, Arragas and Vinas, have dealt with the same phenomena, and have referred the food waste and resulting starvation to a primary impairment of the pancreatic function. And it is significant to note that cases analogous to the infantilism described by Herter as of intestinal origin have been reported by Bramwell and by Rentoul, and by them considered as due to failure of the pancreatic function.

From the study of a number of such cases, three of which are here reported, it has seemed to me that the apparently conflicting opinions as to etiology can be brought into unionism.

DUODENAL ORIGIN

There is evidence to support the contention that the primary lesion in these cases is an infective duodenitis with a secondary invasion of the pancreatic ducts and the production of pancreatic insufficiency, and the assumption of this theory has suggested a therapeutic procedure for the severe cases that seems worthy of further trial.

The rôle of the pancreas in fat-splitting is so well demonstrated that there is no need to quote the various physiologists and clinicians who have written on this subject. There seems to be a general consensus of opinion that if more than one-third of the fat ingested appears in the stools unsplit — that is, in the form of free fats — or even if such a proportion carries material quantities of fatty acids, the steapsin of the pancreas may be considered to be either insufficient or inefficient.

This view is opposed by Vaughan Harley who holds, from the study of a case of pancreatic obstruction, and from experiments on depancreatized dogs, that when excess of fat appears in the evacuations, diminished absorption, rather than deficient splitting, is the lesion. He came to this conclusion because, in his cases, a small proportion of fat was absorbed, but a large part of the waste appeared as fatty acids and soaps. He further feels that the pancreas has some internal secretion, as yet undis-

covered, which is active in the absorption and utilization of fat, and this view is borne out by the experiments of Gross and of Falta. It is well understood that pathologic conditions in tissues other than the pancreas can lead to a large waste of fat in the stools. In acute duodenitis with jaundice, in certain diseases of the liver in which biliary secretion is suppressed, in chronic tuberculous mesenteric adenitis, and in any acute enteritis, stools bulky with wasted fat may be encountered.

Talbot, in an interesting paper on tuberculous mesenteric adenitis, reports but one case in which the bowel movements contained any large amounts of free fat or fatty acids. In the major number of his cases, the fat excess was in the form of soaps, and his observations coincide with my own and with those of most observers. These findings indicate that the fat has been split, but that the absorption is inadequate. The few reported cases that show deficiency of fat-splitting can be explained on the ground that there is a partial or complete blocking of the pancreatic duct by that group of glands which lies about the head of the pancreas, where inflammation or enlargement might affect the duct by contiguity.

An interesting description of the rôle of the pancreas in splitting and absorbing fat, with an account of an unusual case of steatorrhea persisting from birth in an otherwise healthy child, one of whose five brothers was similarly affected, is contained in a paper by Garrod. The author assumes an inborn failure of fat-splitting power on the part of the individual reported on.

It seems also to be clearly demonstrated that one of the three pancreatic ferments, the lipase, the amylase, or the alkali protease may be diminished in quantity or power, while the other two secretions of the gland are doing their work in a fairly normal manner. A paper by Gross discusses this subject fully in its relation to the adult pancreas, but there seems to be no adequate study of the difference between the secretory power of the young pancreas and that of age.

The fact that bacterial invasion of the pancreas happens through the ducts as well as by the blood-stream, by the lymphatics and by contiguity (especially from infected mesenteric glands), is one of the best demonstrated facts in medicine, for acute suppurative pancreatitis, which one hears of rarely in childhood, has been reported to have been produced by the colon bacillus, the streptococcus, the staphylococcus, by mixtures of these two organisms, by the pneumococcus, by the bacillus of Friedlander and in rare cases by the typhoid and paratyphoid organisms. Invasion is

determined by two facts: 1. By the production of much mucus at the ampulla of Vater, which causes partial blocking. It has been shown that under such conditions of stagnation the bacteria, especially motile bacteria, can readily ascend any of the body's various ducts. Bond's work on ascending mucus currents is of particular interest in this consideration. He has shown that when epithelium is damaged, inert particles can ascend ducts lined with mucous membrane, and he has suggested that this is a common mode of ascending infection by bacteria. 2. The second determining factor was pointed out by Carnot, who has made a thorough study of pancreatitis. He demonstrates that blocking allows pancreatic enzymes to act on the epithelium lining the ducts and to soften and destroy it, and so provides pabulum for the organisms imported from the gut.

As long ago as 1898, Arraga and Vinas, in a detailed study, showed that it is not rare to encounter a more or less complete blocking of the pancreatic duct of children, with invasion of the duct by intestinal bacteria. Herter has shown, however, that at the level of the upper portion of the duodenum there are normally very few or no bacteria, and that these, when they do occur, are not of the pathogenic type. The inference is, then, that any invasion of the pancreas is secondary to a duodenitis in the presence of unusual bacterial forms in the upper gut.

BACTERIOLOGY

The type of case that this paper deals with cannot, of course, arise from acute suppurative pancreatitis, but if the possibility of ascending infections be accepted, as it is by all those who have carefully studied the matter, it is conceivable that bacteria of low pathogenic power ascending the ducts under like conditions will give rise to low grade of inflammation, followed by fibrosis, greater or less in degree. As a matter of fact, this is just what does happen, and such conditions found post-mortem in the pancreas have been attributed to invasions by colon bacilli of low resistance, to the staphylococcus, and to other pathogenic germs whose powers to damage their host had been minimized by residence.

On the other hand, organisms whose virulence is never great may establish themselves in the intestine. In the condition of acute and subacute infection already referred to as described by Herter, fecal fields instead of showing the normal preponderance of Gram-negative bacilli of the colon group, exhibit a bacterial flora similar to that seen in the stained fields made from feces of normal breast-fed nurslings. That is,

the bacteria in these fields present the morphological characteristics of the simple form of the *Bacillus bifidus*. In some of these cases, a bacillus described by Herter and Kendall as *Bacillus infantilis* is present. There is some doubt as to the exact position this organism should take, and even Herter was of the opinion that it might possibly be a form of the *Bacillus bifidus*. Herter was interested in these cases chiefly because of the likeness the intestinal flora showed to the flora he found in those cases of infantilism that he studied and grouped as of intestinal origin.

The study of the stools in the group of analogous cases reported by Dr. R. G. Freeman, showed that in some the same types of *Bacillus bifidus* were predominant, and in others, one case in particular, Welch's *Bacillus aerogenes capsulatus*, occurred in preponderance with no *B. bifidus;* in another, it was found in company with the latter organism and other bacilli.

When one considers that although steapsin is obtainable from the intestinal mucous membrane and from many other tissues of the body, the possibility of another lesion than that of the pancreas must be admitted in the case of those patients who waste fat so considerably, but that the pancreas should not be involved is unlikely even if other tissues are at fault. As a matter of fact, the post-mortem records of Arraga and Vinas reveal that in children who have shown such clinical pictures, there has been invasion of the ducts with evidence of chronic inflammation around the ducts; they describe the pancreas in these cases as being remarkable for the diminution of its volume, its increased hardness, its toughness on section and for definite marking out of its lobules in which the normal differentiation is markedly exaggerated. They say that throughout the essential tissue minute areas of degeneration and hemorrhage are found dotting the lining membrane of the ducts, and that there is a great increase of viscid mucus within these ducts. They describe the microscopic picture in these words:

> If we examine the duct of Wirsung at or near its entrance into the intestine, we are struck in many cases by the fact that the lining epithelium has almost disappeared. The wall of the duct is markedly thickened and is made up of fibrous striae surrounding collections of leukocytes. There is also in the new connective tissue a very marked increase in the number of blood-vessels, and these, for the most part, are unduly dilated. In the less severe cases, the process is not so advanced and we are able to see the epithelium in the process of degeneration; there is softening of the cells, with a fragmentation of the nuclei which gives rise to a poor staining reaction. Many of the cells are in the process of desquamation and are contributing to accumulations that block the ducts. A thorough examination shows that the degree of damage is proportional to the

duration of the disease. From the finer ducts which have been attacked, widespread invasion of the parenchyma of the pancreas takes place, and is followed by a connective tissue increase. Following this increase of tissue, one finds secondary changes in the pancreatic acini, some of whose cells undergo softening, and others coagulation necrosis, with nuclei of lost contour, and poor staining quality. These lesions are most frequent in that portion of the pancreas neighboring the outlet of the duct of Wirsung. In those instances in which enteritis has been persistent and of long duration, a marked dilatation of the veins of the pancreas may be seen.

These authors look on the *B. coli communis* as the probable invader in these cases. They consider its motility as an important factor in aiding its entrance to the pancreas, but when we consider the work of Bond already referred to, there is no reason to doubt that any organism, motile or immobile, can invade the pancreas.

It seems perfectly reasonable, then, to assume that in the cases of patients whose stools show marked increase in free fat waste, definite depression of those digestive powers usually attributed to the pancreas, and in the stool a predominance of abnormal bacteria, the ducts of Vater, and through them the pancreatic tissue, has been invaded by these abnormal organisms, and the pancreas has undergone an inflammatory reaction which has damaged the secretory power of the gland and impaired the digestive quality of its juice.

The autopsy of one of the cases here reported seems to warrant such an assumption, and the clinical findings in another also indicate the probability of this pathologic complex. The fact that many of these patients automatically recover is no argument against this contention, because it is quite conceivable that certain mild cases may be due to the establishment in the upper intestinal tract of a bacterium that maintains itself in this region with difficulty. Unless invasion of the pancreas occurred very rapidly, such an organism would find that the body had adapted its protective powers in the way that happens so frequently when the colon bacillus invades the urinary tract. Again, following dietetic measures, or the use of saline or mercurial purges, inflammation in the intestine may be allayed, mucus accumulations obstructing the outlet of the ducts cleared away, and the conditions which favor invasion of the pancreas by bacteria changed. The fact, therefore, that many cases have improved on simple dietetic treatment, or after the use of mercurial purges, is perfectly in accord with the view of the etiology here set forth.

The following examples of cases met in practice will be used to emphasize the contentions made in this paper.

CASE REPORTS

CASE 1.—Stella S., aged 22 months; weight 17 pounds. At the age of 1 year she suffered from an attack characterized by frequent, loose bowel movements, without pain, tenesmus or fever. This attack lasted for about ten days and she had no more trouble until February, 1911, when she had a recurrence of the same conditions in a more severe form; this attack had lasted for about three weeks when the child was first seen on February 27.

Physical Examination.—The child was then wasted and irritable. Hair was ill-developed and she had a distended belly; no fluid was found in the peritoneal cavity. The tonsils were not enlarged; there was no clinical evidence of lues; the Wassermann test was negative. The stools were characteristic, bulky, grayish-white, greasy bowel movements. The attending physician stated that she had had very marked starch waste.

She was put on a diet of 800 calories a day, provided through dextrins, skim milk, gelatin, scraped beef or white fish, maccaroni or rice, with green vegetables and fruits.

The report of the stool examination showed that on different occasions there was a great excess of free fat and fatty acids with some soaps; a moderate number of starch granules, both free and encapsuled were found. The blood showed 75 per cent. hemoglobin, 12,000 white cells, 58 per cent. lymphocytes, 42 per cent. polymorphonuclears; no parasites.

On July 20 there was no free starch in the stool; neutral fats and fatty acids were present in excess; the bacteria were predominantly Gram-positive; no colon bacilli.

August 29 a large amount of starch was being wasted; it seemed there was no fat in one examination, but the Gross casein method and Wohlgemuth starch test gave a very marked diminution in the amylase and protease of the stool.

September 6 there was a considerable excess of starch and of free fat; casein and starch digestion by the above methods was very much improved — from 100 units at the first examination, to 375 at the last. The child in the meantime increased in weight and well-being; her appetite improved and October 4 her weight was 24½ pounds. Since that time she has made a steady gain in weight and health and has shown no tendency to a recurrence. On the last examination of her evacuation by Dr. Alvarez, fourteen months after she was first seen, there was no excess of fat, free starch was not present, and the normal Gram-negative colon bacilli were reported as being predominant in the stool.

This is an example of a mild and temporary pancreatic insufficiency which is not at all uncommon to meet in infants of this child's age, and which, it seems probable, is due to a bacterial invasion of the intestinal tract and an ascending infection of the ducts of the pancreas. It is an upset which rights itself when under proper feeding conditions, the unusual bacteria give way to those normal to the small intestine, which under ordinary conditions are unable to grow with any amount of vigor so high up as the opening of Vater's duct. There are a number of cases in our history files which duplicate this in all its essential particulars.

The following case is an extreme example of the same condition:

CASE 2.—A. H. was first seen in his twenty-first month. Then he weighed 14 pounds, an increase of but 7½ pounds since birth. His mother's statement was that he had been breast-fed for the first four months, and that during this period he had gained one-half pound a week; from the fourth month he gained but little and at 9 months ceased to gain, but seemed contented and happy until during his tenth month he began to vomit; during the attacks he brought up at first food, and later large quantities of sour-smelling, bile-stained, watery material. There was then a period of improvement which lasted four months, although at that time he was on a diet that apparently contained about 5½ per cent. of fat. He then developed an alimentary intoxication, when he was seen by another physician who withheld all food save skimmed milk. Under this regime a slight improvement followed with a gain of a few ounces a week. At the age of 16 months he began to stand and was steadily gaining strength, up to his twenty-first month, when I first saw him in a vomiting attack similar to those already described.

Physical Examination.—The infant was found to be suffering from marked scurvy which rapidly disappeared when he was fed fruit juices. He was emaciated, with an exceedingly protuberant belly. Examination revealed nothing abnormal in nervous system, heart, lungs or abdomen, except marked distention, which was obviously due to intestinal gas. Neither spleen nor liver was enlarged; there was no fluid in the peritoneal cavity and no enlarged glands present. The blood showed no lymphocytosis, the hemoglobin was slightly diminished, no nucleated cells were present, but there were some alterations in the size and shape of the cells. The child vomited a large quantity of bile-stained fluid mixed with mucus and smelling of fatty acids. He would vomit from 1 to 2 quarts of this material daily during the attacks, which lasted from two to five days; during these periods the urine was scanty and concentrated. He had from two to three foul stools daily. When first seen these stools were scanty and composed largely of mucus; between the attacks of vomiting the stools were large and greasy, and contained large amounts of free fats and fatty acids. There was no starch reaction to iodin; no muscle fibers were found present; this examination was made some days after the child had been on a mixed diet of green vegetables, broth and scraped beef, with minimum amounts of fat. The urine at this time and in subsequent examinations showed a heavy indican reaction, and Ehrlich's aldehyde reaction was positive, but neither albumin nor casts were found. On a mixed diet, with the exhibition of gray powder, ½ grain three times daily, the stools improved, the general condition was better and there was no further vomiting.

Management and Course.—In his twenty-eighth month the child suffered an attack of whooping-cough through which he passed uneventfully and from which he recovered without complications. After this he gained at the rate of about 1 pound a month until he weighed 18½ pounds. During this time no deficiency in the digestion of starch or protein was demonstrated by the Gross or Wolgemuth tests, but diminution in the pancreatic steapsin was to be inferred, as the fats were apparently entirely unsplit and unabsorbed. Unfortunately, no quantative determination of the relation between the ingested and excreted fat was made. Under the most careful and searching clinical observation by me and by Dr. Charles Minor Cooper, no indication of any complicating disease could be determined; the digestive tract only could be implicated.

The child's appetite was extremely capricious and it was difficult to get him to take a sufficient amount of food. On two separate occasions there was a definite color change in Fehling's solution when boiled with the urine. The change did not occur immediately and there was no true precipitation.

In his thirty-second month there was a very marked acceleration of all the symptoms. The patient, who had been improving and was allowed some freedom in diet, was seized with a characteristic diarrhea, having four to five stools a day. These were fetid, fatty-acid odored, greasy, and under the microscope they showed quantities of unsplit fat. This in spite of the fact that the fat was limited in the diet. During this attack, for the first time, starch appeared unaltered in the stools and meat fibers were discovered undigested, although meat was given in the form of very thoroughly scraped beef. At this stage an emulsion of raw sheep's pancreas was given with apparent effect. The child improved in strength and digestive power and returned to a limited degree of comfort, and again began to gain in weight. A light attack two months later was checked, whether spontaneously or through the aid of the pancreas emulsion, one is not certain. Pancreon (Rhananier), which it was attempted to give this baby, was always vomited. During the period of pancreas feeding, the pancreatic nuclei were always passed undigested and could be seen in great numbers in the stool.

At all examinations the fields of fecal flora showed a preponderance of Gram-positive cocci and bacilli which were reported as not unlike Boas Oppler bacilli, but smaller. At that time we attached no importance to the presence of these organisms in the digestive tract.

When the child was within a month of completing his third year he again became the subject of an attack which proved fatal. At this time he was not under direct observation, but the mother, a very intelligent observer, declared that on several occasions he passed voluminous stools of tarry material, which description seemed to indicate hemorrhage from the intestine, although the autopsy records showed that no blood was found in the intestine after death.

Necropsy.—The child died at 7:15 p. m., Sept. 18, 1911. Autopsy was permitted, but was not done until noon of the following day. The autopsy records state that the post-mortem revealed a very wasted child, the body in marked *rigor mortis*. On opening the belly, the intestines were pale and moderately collapsed. The ascending part of the duodenum was hard and seemed fibrotic. No fluid in the peritoneal, pericardial or pleural sacs; retroperitoneal glands slightly enlarged, not inflamed. Liver slightly decreased in volume, somewhat hard, spleen normal; right kidney larger than the left. The pancreas lay across the spine as a hard cord about the size of the little finger, was pale in color, but did not tear easily. Unfortunately, no examination was made of the papilla of Vater nor of the condition of the ducts. No enlargement of the mediastinal or bronchial glands was found. Lungs free from adhesion, pale in color, did not tear easily, left apex firm to the touch, but floated in water. Heart in systolic contraction, normal.

Microscopic Examination (by Dr. William Ophüls).—Pancreas showed increase in connective tissue of septa: slight interlobular increase; pancreatic tissue was fairly abundant and seemed normal in appearance; there were many islands of Langerhans. Kidney showed slight increase of connective tissue in cortex; tubules normal; glomeruli normal. Lungs showed some areas of collapse where lining epithelium was cubical; otherwise normal. No abnormal changes in the intestine. Diagnosis: Pancreatic fibrosis; slight interstitial nephritis.

CASE 3.—This paralleled the last described in all the features except outcome. B. J. When the child was 13 months of age her mother noticed an abnormal distention of the abdomen; a week later vomiting with fever ensued and lasted two days: the stools, four to six daily, were then gray, smooth and voluminous. When first seen she was 17 months old. It was related that she was losing weight steadily.

Physical Examination.—The child was moderately grown, poorly nourished, much wasted; abdomen distended, not very full in the flank; bimanual examination made under anesthesia per rectum disclosed no tumors and no enlargements of the viscera. Reflexes, heart, lungs and throat normal. Blood, 10,200 white cells with a normal differential count. Hemoglobin 65 per cent. Von Pirquet tuberculin test was negative. Stools showed abundance of fats and fatty acids, some soaps, meat fibers, starch, dextrin and nuclei. Bacteria, Gram-positive bacilli in predominance. Urine usually normal; on two occasions showed slight sugar reaction; occasionally gave a marked indican reaction; the stools showed a moderate Ehrlich's aldehyde reaction; on a number of occasions a slight trace of albumin was present; at several times a few granular and hyaline casts were seen. Acetone was occasionally found during periods of starvation, and the same Gram-positive bacterium that dominated the stool was found in the urine several times; this was probably due to contamination. During the pancreas feeding an enormous amount of uric acid was reported as being present in the urine.

Course.—The child went progressively from bad to worse, and no food was tolerated by the intestine until Loefflund's malt soup, prepared with skimmed milk, was tried, and even with this aliment undigested casein was present in the stools. The weight fell steadily until it was less than 10 pounds. The clinical picture of extreme starvation with irritability was most pitiful. During this time the stools continued to show the Gram-positive bacillus in practically pure culture.

Bacteriology.—Dr. Alvarez' report is as follows: Escheric stain shows almost pure culture of a Gram-positive bacillus, often slightly curved, not as long as the Boas Oppler (probably not *Bacillus bifidus*). Fermentation tube culture shows a large amount of gas with a strong odor. Sediment shows a large number of the Gram-positive bacilli seen before and large amount of proteins; no signs of *Bacillus bifidus*. Acid bouillon shows no growth in ferment tube.

Emulsion of raw pancreas was given without apparent effect on the digestion; in fact, the amount of fat contained in the pancreas seemed to make matters very definitely worse, and unsplit fat appeared in the stools. With the hope of stimulating secretin, hydrochloric acid was now given without any change in the stools. Shredded pig's duodenum was now used in the attempt to provide a secretin, but without success.

Vaccine Treatment.—Dr. Walter C. Alvarez, to whom I am indebted for the laboratory examinations in this case, suggested that the constant domination of the stool by a Gram-positive bacillus was presumptive evidence of the pathogenicity of this organism, and proposed that an autogenous vaccine be prepared and given to the child. This was done. The report of the first culture of this organism is as follows:

Culture on agar shows very minute white colonies which are apparently pure culture of the Gram-positive bacillus. They grow occasionally as long threads, or again as diplobacilli. On bouillon, the Gram-negative organism predominates by far. Transplant from agar to agar shows marked change to a thick diplo-

bacillus sometimes so short as to be a thick diplococcus in chains; a few are Gram-negative and some may have spores.

The vaccine was prepared from the agar culture and every third day was given to the child in increasing doses, beginning with ten million. Up to this time the reports of stool examinations showed absence of diastase, low trypsin and practically no fat digestion; diastase was also absent from the urine.

No change was observed in the child for five days, when a fair amount of diastase was reported as being present in both stool and urine. The next examination, five days later, showed that there was still an excess of starch in the stool, but more than the usual number of Gram-negative bacilli, although there was still a large number of Gram-positive organisms. Subsequent examinations showed variations, diastase increasing in the stool, and starch varying from none to a slight excess, in one instance a large excess; free fat, fatty acids and soaps decreased in quantity, although whole milk was added to the dietary.

Three months after beginning the vaccine treatment, after about thirty injections, there were very few Gram-positive bacteria present, and the stool contained considerable soap. Five months after the beginning of the treatment, after an unremitting improvement, the child was able to take a normal mixed diet with a moderate amount of fat without any excessive waste; the stools showed simply a high predominance of soap, no wasted starch and a normal bacterial picture. By this time the child weighed 21½ pounds and was apparently in good general health.

CONCLUSION

It may be concluded then, that in the group of cases characterized by waste of most of the ingested fat, with or without loss of the ingested starches and proteins, we are probably dealing with a bacterial invasion of the pancreas secondary to the presence of an abnormal bacterial flora in the small intestine. The material here presented is too scanty to expect conclusions drawn from it to be accepted as final; the paper is prepared with the hope that others may consider it worth while to investigate the condition from this point of view.

The question of the value of vaccines in such a condition is brought up because in one case the results following the use of a vaccine were so striking that it seems impossible that mere coincidence will explain them. It is not suggested that one certain organism is specific for this condition. It seems quite reasonable that any pathogenic bacterium, or even the colon bacillus, under abnormal intestinal conditions, may become the inciter of a pancreatitis which may lead to a suppression or deficiency in one or the other of the pancreatic ferments.

Undoubtedly, a large number of cases in this group are mild and transitory and will respond to such dietetic measures as make the intestine an ungrateful field for the growth of the organism pathogenic in the particular case.

Schroth Building.

DISCUSSION

DR. PORTER: In conclusion I wish to say that finally after several ameliorations he died. The pancreas was about as large as my little finger and very hard. The other case was that of a smaller child. As the child was constantly losing weight, he was kept alive by maltose administered as malt soup. We made a vaccine from the pancreas bacillus merely in the hope of doing something for the child, although we had no scientific basis for doing so. The laboratory reports show an entire absence of diastase, low trypsin, and practically no fat digestion. Diastase was also absent from the urine. Whether or not this was a coincidence, I cannot say, but the bowel movements began to decrease. The child was wasting a large quantity of fats and fatty acids. The vaccine was given in doses of ten millions and was increased to fifty millions, given three times in injections. The child to-day has improved in health and seems to be a perfectly normal child weighing 22 pounds.

A RAPID CLINICAL METHOD FOR THE ESTIMATION OF TOTAL FAT IN INFANTS' STOOLS *

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One of the great disadvantages in the study of the digestive disturbances of infancy is our inability to determine quickly the quantity of fat present in an infant's stool. Qualitative tests, while of value, do not suffice, for under normal conditions we may encounter neutral fat, free fatty acids and soaps in an infant's stool. Our requirements will not be fulfilled until we have some approximate method for determining the neutral fats, free fatty acids and the soaps as they exist in the stool when it leaves the body, or, in other words, as they exist in the intestine uninfluenced by external agencies.

In pursuance of this need we began last September to study the various methods now in use for the estimation of fat in stools with the hope that we might find a way of shortening some of the existing methods, or of combining the different principles involved into a new or modified method. The methods we have investigated more in detail are the Kumagawa and Suto, Friedrich Müller, Keller's modification of Röhmann's and the Folin-Wentworth method. Hoffman's copper acetate method, a qualitative method with approximate relative quantitative possibilities, did not give us satisfactory results.

From our investigation we believe the Folin-Wentworth method comes the nearest being accurate of any of the methods considered. We base our opinions not on long or continued use of any of these methods, but on the principles involved. The Folin-Wentworth method, however, does not give us what we want. It determines only the neutral fat, the fatty acids, including the fatty acid of the soaps, and the total fats. If we regard the free fatty acids in the stool of little importance, as some have done, we may then regard the figures obtained for fatty acids as representing the soaps. We believe, however, that we are not justified in disregarding the free fatty acids, for under some conditions they are not insignificant. The Folin-Wentworth method is not a clinical method. It requires from twenty-one to twenty-four hours to complete it, provid-

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ing the extracting apparatus can be kept running the full twenty-hour period. It is suitable for careful metabolism work, but even here there are times, as we shall show later, when it fails to extract all the fat from a sample of stool.

One of us had been endeavoring for some time to develop a centrifugal method for the estimation of total fat. Being unable to get uniform results, we abandoned this method and directed our attention to an investigation of the rate of extraction with acid-ether according to the Folin-Wentworth method. Our results will be found in Table 1.

TABLE 1.—RESULTS OF EXTRACTION OF FAT FROM STOOLS BY THE ACID-ETHER METHOD

Sample 3. Pulverized Stool After Extracting.	Neutral Fat, Per Cent.	Fatty Acids, Per Cent.	Total Fat, Per Cent.	Total Fatty Substance, Per Cent.
Fractional Experiment*—				
One hour	1.73	17.69	19.42	37.20
Five hours more	0.02	22.36	22.38	42.87
Fourteen hours more	0.50	9.90	10.40	19.92
Total	2.25	49.95	52.20	99.99
Sample 3 extracted the full twenty hours	4.49	45.49	49.98	.....
Difference in total result...	+ 2.24	— 4.46	— 2.22	.....

* In this experiment a new weighed flask was substituted at the end of each run. The extraction was kept running the full twenty-hour period.

From this experiment it will be seen that the bulk of the neutral fat appears to be extracted at the end of the first hour, and the bulk of the fatty acids (produced by the action of the acid ether on the soaps) is extracted at the end of the sixth hour.[1] In other words, 76.88 per cent.

1. The formation of fatty acids from soaps is what is termed a substitution process. It is readily effected with weak acids. The following experiment shows how completely the acid ether extracts a sample of soap. We took of

Pure castile soap, gm	1.1035
Extracted 12.5 hours with N/10 acid ether. Weight of substance after extraction, gm	1.1142
Weight of substance unextracted by petroleum ether, gm	0.0412
Fatty acids recovered from the soap. By subtraction, gm	1.0623
By titration, gm	1.0516

of the neutral fat comes out in one hour, 82 per cent. of the fatty acids in six hours, and 80 per cent. of the total fat in six hours. It will be further observed that in the sample undergoing undisturbed extraction for twenty hours, over twice as much neutral fat is obtained and the amount of total fat is over 2 grams less than that obtained in the fractional experiment. From this we conclude that the cold acid-ether process of extraction cannot be utilized for clinical purposes in the sense of giving us data on the three varieties of fat encountered in an infant's stool. We thought some importance might attach itself to the fact that the bulk of the neutral fat came out during the first hour's extraction, but the difference between the neutral fat figures for the fractional extraction experiment and the undisturbed twenty-hour extraction experiment is so great we feel that this process cannot be depended on for quick estimation of the neutral fat in a stool.

We next set ourselves the task of endeavoring to shorten the drying period. We encountered stools which dry more readily than others, and stools, which, in spite of many hours drying in the closed hot-air oven and subsequently many months (nine) desiccation over H_2SO_4, fail to remain in powdered form after passing through a forty-mesh sieve. We constructed a drying oven[2] through which a constant current of hot air passed, the stool sample being placed on a shelf over and under which the air circulated. By this method we were able to reduce the drying time one-half. Drying the stool with alcohol also shortens the period, and in many instances, but not in all, this method proved to be the shorter one. By this means the water is taken out with the boiling alcohol and the alcohol finally carefully evaporated off.

After the trial of other methods of extraction, hot alcohol, etc., and titration methods without, as yet, satisfactory results, we again turned our attention to our centrifugal method which determines the total fat only. At times we had succeeded in removing comparatively large amounts of fat from infants' stools by this method, while at other times

2. The oven is easily constructed. One length of Russia iron pipe 3½ to 4 inches in diameter is connected at each end with a circular elbow. At one end the elbow is turned down over a Bunsen burner, at the other the elbow is turned up and a thermometer suspended in it by means of a wire. An opening about 5 inches long is cut into the side of the pipe length and the flap turned into the pipe to form the shelf. A lid or door is hinged above the opening and is kept closed by means of a simple turn catch attached to the lower edge of the lid. The catch fits into a hole punched in the outer edge of the shelf flap. A brisk current of hot air passes through the pipe and the temperature is easily regulated with the ordinary Bunsen.

with samples of the very same stool, and apparently exactly the same manipulations, we got only blank or negative results. The principle of the centrifugal method is the conversion of all fat and soaps into fatty acids, which are later brought into the graduated stem of a centrifugal tube and the amount in cubic centimeters read off directly.

In our effort to obtain uniform results three difficulties presented themselves:

1. A whitish substance almost invariably appeared floating on the surface of the centrifugalized fluid, and later it appeared below or intimately mixed with the fat column in the stem of the tube after final centrifugalization. In some samples of stool in which no fat was present this substance rose to the top and sometimes resembled quite closely a poor fat layer.

2. Carbonization of the fat layer frequently took place because of an excess of acid. After a number of trials on different stools we were able to determine the maximum and minimum amount of acid necessary to burn the organic matter other than the fat and set the fat free, and to work out an optimum concentration which seems to be adaptable to most stools.

3. At times the fat column was difficult to read.

After milk fat passes through the intestinal canal certain physical changes take place. Before ingestion a centrifugal test shows a clear, fluid, yellow fat layer, which becomes more firm as it cools. It remains, however, in this clear condition for several minutes and is easily read. After the milk passes through the digestive tube a centrifugal test shows a denser and darker fat layer, which solidifies at a higher temperature and contracts in such a way as frequently to cause it to break in the center. A reading made when first taken from the machine is frequently a little greater than it is a minute or two later. If the tube is immersed in hot water the fat column melts and again occupies its former position in the tube. There is evidently a change in the specific gravity of the fat after it has passed through the intestinal tube. This difficulty seemed to be almost as insurmountable as the first one, which we will return to later. We thought to alter the specific gravity (lower the melting point) of the fat present in the stool by adding a known quantity of a fatty acid of low melting point. By deducting the difference in the result obtained we hoped to find the total fat content. We chose *oleic acid*. We were able to recover from stools and substances free from fat the amount of oleic acid added, and in stools with a fat content we were able to recover

the oleic acid plus additional fat from the stool.[3] The fat column was by this means made clear. Such a method we believe is not acceptable from a chemical or clinical standpoint, for we are introducing a factor. The introduction into a stool of a substance sought might easily lead to error. We found, as we have stated, that much of our trouble with the fat column came from carbonization induced by adding too concentrated acid.

At this point in our investigation we came across Kita's[4] work on a similar method for the estimation of fat in meat. He had encountered the same difficulty with the appearance of a white substance on the top of the centrifugalized fluid, and found by adding a small amount of amyl alcohol complete separation of the fat layer was effected. We found this to be the case when we added amyl alcohol to our stool mixture. As is quite generally known, the addition of a small amount of 80 per cent. ethyl alcohol straightens out the fat column in the determination of fat in cheese by the Babcock method so that it can be easily read. Our experience with ethyl alcohol, however, has not been satisfactory. Because of its low boiling point (78 C.) when it is added to the hot acid stool mixture, some of the contents are often blown out through the stem of the tube. Kita gives no explanation for the use of amyl alcohol. The alcohol in either case effects a better separation of the fat, and we believe the advantage gained from the use of amyl alcohol lies in its very high boiling point (131 C.). By means of the addition of amyl alcohol, our fat layer now became as clear as we could wish it to be. By immersing the tube in hot water after centrifugalization the amount recovered is easily read off. As a precautionary measure we found it necessary that the amyl alcohol should be thoroughly mixed with the acid water stool mixture, otherwise it would come up into the stem of the tube, and, because of its acquired yellow color, appear as a fat column. We have worked out the following method, which has given us very uniform and apparently quite accurate results:

CENTRIFUGAL METHOD FOR ESTIMATION OF TOTAL FAT IN INFANT'S STOOLS

The Sample.—If pulverized stool is examined, one-quarter (0.25) gram should be carefully weighed. If fresh or moist stool is examined, one-half (0.5) gram. An inexpensive prescription balance is sufficiently accurate for clinical purposes. For more careful work an analytical

3. See foot note to Table 2.
4. Kita, T.: Arch. f. Hyg., 1904, li, 165.

balance is of course necessary. The stool, if dry, is best weighed in a poised watch glass and transferred to glazed paper. Moist stool is quite easily removed by means of a spatula from glazed paper on which it is weighed, or from the watch glass, by means of water. The sample is carefully rubbed up in a thin-lipped mortar. A maximum of 20 c.c. of warm (40 to 50 C.) distilled water is used to transfer the mixture to a Babcock milk bottle graduated in *fiftieths*.* A little practice enables one to transfer the entire sample with the first 10 c.c. of water, leaving the remainder to rinse off the mortar and pestle.

1. To the sample, now thoroughly mixed, 17.5 c.c. H_2SO_4 (1.84) is added. Great care should now be taken to mix thoroughly by shaking the bottle back and forth vigorously (it should be remembered that all the organic material except the fat must be completely burned, or the test will be a failure).

2. One c.c. amyl alcohol is now added and thoroughly mixed.

3. The tube is now carefully counterpoised and centrifugalized for three minutes at high speed. Enough hot water is then added to bring the fat into the graduated portion of the stem of the bottle. The bottle is again counterpoised, centrifugalized for one minute and the number of divisions on the stem occupied by the fat read off. Care must be taken to keep the stem hot and all readings must be made while it is hot. This is quickly accomplished by immersing the bottle in a pitcher or beaker of hot water.

Calculation.—If 0.25 gram of stool has been used, multiply the number of divisions on the stem of the tube occupied by the fat column by the factor 7.2; if 0.5 gram sample of stool is used, multiply by the factor 3.6; the result is the percentage of fat in the sample examined.

To determine the amount of fat in the twenty-four-hour sample of stool, the stools may either be weighed when passed, or they may be kept in a moist chamber and weighed at the end of the period. The former is the better method, for, by this means any loss or gain in weight may then be detected and accounted for. The stool from which the sample is taken must be thoroughly mixed. From the known weight of the

* We have adapted the method to glassware easily obtainable. A Babcock 8 per cent. milk bottle should be selected. Each per cent. in this bottle is graduated in tenths. From 0 to 5 per cent. contains one c.c. and is accordingly divided into *fiftieths*. The stems of Babcock bottles graduated from 0 to 10 per cent. hold two c.c. Each c.c. is divided into twenty fifths. If this bottle is used the *factor* employed must be multiplied by two.

stool the total amount of fat is readily estimated. With a little practice a complete test can be made in ten minutes.

Sensitiveness of the Centrifugal Test.—Table 2 records a few comparative tests with the Folin-Wentworth method.

TABLE 2.—COMPARISON OF CENTRIFUGAL METHOD WITH FOLIN-WENTWORTH METHOD

Stool No.	Food Given.	Character of Sample	Percentage of Fat Obtained by the						
			Analysis No. Centrifugal Method.				Folin Wentworth Method. Analysis No.		
			1	2	3	4	1	2	3
1	Eiweissmilch..	Pulverized.	36.00	36.00	36.00	.....	36.32	.....	.....
3	Eiweissmilch..	Pulverized.	43.08	43.23	.....	.....	49.98	52.20	.....
8	Eiweissmilch..	Pulverized.	36.00	32.40	32.40	32.40	34.52	35.24	.....
9	Breast milk...	Moist*	16.20	16.20	16.20	16.20	.....	.....	.....
11	Breast milk...	Pulverized.	50.40	50.40	50.40	.....	34.70	35.30	34.60
							Centrifugal test on sediment left in extraction capsule.....		14.40
									49.00

* Oleic acid method. By substituting 0.1 c.c. oleic acid for the amyl alcohol and rubbing it well into the stool we obtained with a sample of this stool 34.20 per cent. fat. Subtracting the oleic acid value, 18 per cent., we obtained exactly the same result, 16.20 total fat.

It will be observed that in most instances the centrifugal method gives practically the same reading on the same stool. It is not subject to as many variations as the extraction method. It will be further observed that for some unexplained reason at one time it gave a lower percentage than the extraction method. In another rather striking instance the centrifugal method gave a much higher reading than the extraction method. In the last instance we were able to demonstrate that the acid ether failed to extract 14 per cent. of the fat after twenty-six hours' extraction in the Sohxlet apparatus, and that the addition of this amount to that previously obtained by the extraction method was almost

the same as the figures obtained by our centrifugal method. Furthermore, in the case of the third analysis (No. 11), Folin-Wentworth, only 0.5 gram sample of stool was used and run for twenty-six hours, which is the equivalent of fifty-two hours on 1 gram, and yet we were able to extract no more fat than in the other two cases.

We believe the true fat content of this sample of stool would not have been known had we depended on the Folin-Wentworth method. This is the breast-milk stool previously referred to, which resisted pulverization, even after nine months' drying over H_2SO_4. After rubbing this sample through a fine sieve, it persisted in forming little balls and coffee-ground-like masses. These doubtless resisted extraction by the cold acid ether. The hot acid water mixture of course readily overcomes this difficulty. In the one case extraction is at work; in the other, liberation.

We believe a knowledge of the total fat content of stools may prove to be of value in the diagnosis and treatment of the digestive disturbances of infancy, and we hope this simple method, based on the Babcock principle, will help to further our knowledge in this field of medical research.

IS DIPHTHERIA FREQUENTLY A BACTEREMIA?*

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In August last, Conradi and Bierast[1] of the Hygienic Institute of the University of Halle reported the results of an extensive examination of the urine of diphtheria patients. They call attention to the fact, that, while diphtheria has been regarded as essentially a local disease, yet the Loeffler bacillus has frequently been isolated from the blood and organs after death, and occasionally from the blood during life, usually, however, in the agonal stage of the disease. On account of the technical and other difficulties of obtaining a sufficiently large quantity of blood from diphtheria patients, they sought to solve the question of diphtheria bacteremia by an indirect method, namely, an examination of the urine of those actively ill, and of convalescents. In all, 155 patients were examined, of whom fifty-four showed a positive urine. In six cases only, however, were virulence tests made, all of which proved positive. As the material was sent to the research laboratory at random, there was no possibility of following up a given case in order to study the question of the persistence of the bacilli by repeated examination. Of the 54 positive cases, 32 were female and 22 male; 36 children, 18 adults. Thirty-one urines were taken in the first week of illness, 10 in the second, 5 in the third, and 2 in the fourth. One was found positive in the ninth week of convalescence. The urine, 20 to 30 c.c. in amount, was taken by means of a sterile catheter with every precaution against contamination, and the centrifugalized sediment spread over one or two Loeffler plates and plates of Conradi and Troch. Both Loeffler and Neisser's stain were used for identification. The bacteria were found in normal as well as albuminous urine, showing that they pass through healthy as well as diseased kidneys. In most cases they were very few in number.

No clinical data are furnished in regard to the severity or outcome of the cases giving positive results. On the strength of their findings the authors make a plea for the disinfection of the urine of convalescents, until, by three negative cultures, it is shown to be free from diphtheria

*From the Research Laboratory, Department of Health, New York City.

1. Conradi, H. and Bierast: Deutsch. med. Wchnschr., Aug. 22, 1912, No. 34.

bacilli. They suggest that diphtheria of the skin and mucous membrane, which shows such a predilection for the genital and anal regions, is due to direct infection from the urine, and that the mystery that surrounds the origin of certain local epidemics of diphtheria may be explained in the same way.

Dr. R. Koch[2] of Frankfort, in December, reports the results of his examination of 111 urines from 26 patients. In 4 of these, which came from two patients, virulent diphtheria bacilli were found. In 10 urines from 5 other patients, diphtheria-like bacilli were found, which either could not be isolated in pure culture or else proved to be avirulent. In the original smears diphtheria bacilli were never recognized.

The urine was passed into a sterile vessel after thorough cleansing of the meatus with mercuric chlorid solution. In 74 examinations made on 19 patients suffering from mild or moderately severe diphtheria—in one case 14 examinations were made in 25 days—no suspicious organisms were found. In 5 other patients diphtheria-like organisms were found which proved to be avirulent; 2 of these were fatal cases. Post mortem examination of the urine proved negative.

Of the two positive cases, both ended fatally from the toxemia of the disease and cardiac paralysis. The first showed negative urine on the first two examinations, virulent diphtheria bacilli being found on the seventh day, the patient dying on the following day. In the second case they were found on the fifth day of the disease and the following day, being absent on the next five days and present on the twelfth day again, the patient dying the next day. The appearance of the bacilli in the urine was in neither case coincident with change in the general symptoms. The presence or absence of albumin in the urine had no bearing on the presence of bacilli.

Nineteen cases of scarlet fever complicated by diphtheria were examined as controls. In four of them the urine contained diphtheria-like bacilli which proved to be avirulent. We believe that only animal tests can be relied on for the identification of diphtheria-like bacilli in the urine. While Loeffler bacilli may occasionally occur in very severe cases, the fact is not of practical interest, as such patients, being confined strictly to bed, would not be likely to be a source of danger through infected urine.

2. Koch, R.: Deutsch. med. Wchnschr., Dec. 12, 1912, No. 50.

The latest writer on the subject is Walter Beyer[3] of Rostock, whose reported results are little short of startling. He examined nineteen cases of diphtheria daily, or every second day, from the active stage of the disease to late convalescence. Forty c.c. or more urine were taken with proper precaution against contamination, and the centrifugalized sediment poured over a Loeffler plate. Practically every urine examined showed diphtheria bacilli at each examination; their number being greatest during the active stage of the disease and gradually diminishing. In the case of eight convalescents, four of whom had recovered from their illness, three and one-quarter to three and one-half months previously, and the others eight, six, five and four weeks, respectively, the urine showed the continued presence of diphtheria bacilli, six strains of which were said to have been virulent for guinea-pigs, the other two avirulent. In all of the eight cases cultures from the tonsillar crypts showed diphtheria bacilli. It is to be noted that there is nothing said by Beyer or Conradi as to their methods of testing for virulence; that is, as to whether antitoxin was used in the test.

Beyer believes that it has been established beyond doubt that in the early stages of diphtheria, at least, the disease is essentially a bacteremia. Whether the organisms found in convalescents constitute also an evidence of a continued blood-infection he does not undertake to say.

Our series of cases comprises 54 patients with 56 examinations of urine. These were divided into three groups roughly corresponding to the type of disease which characterize the clinical material from which the three observers quoted obtained positive results. Thus the first group, 25 in number, consisted of routine cases; the second, 21 in number, cases of the severer type with a great deal of membrane and showing symptoms of toxemia; third, 8 in number, cases of recent convalescents. All were patients at the Willard Parker Hospital.

In the first group, there were 5 adults and 21 children, the ages of the latter ranging from 2 to 13 years. There were 18 males and 7 females. Twelve patients were in the first week of the disease, 7 in the second, 3 in the third, 1 in the sixth week and 2 not determined. Only 1 or 2 of these cases were of any severity. The urine proved negative in every case.

In the second group of 21 cases there were 4 adults and 17 children, the latter 2 to 11 years, 16 males and 5 females. Twenty were ill for a

3. Beyer, Walter: München. med. Wchnschr., Feb. 4, 1913, No. 5.

week or less at the time of taking the urine and 1 with croup and cervical adenitis for sixteen days. Two of this group proved positive. One, Edward M., 8 years of age, two days ill, had thick membrane covering the tonsils, fauces, uvula and posterior walls of the pharynx; there was also nasal discharge and marked toxemia. The serum tube and ascitic broth showed Loeffler bacilli which proved to be virulent. A specimen taken one week later was negative. The patient made an uneventful recovery. A second patient, Sam G., aged 5 years, had been ill three days. The patient had thick membrane on both tonsils, uvula and pharynx with profuse purulent nasal discharge. The cervical nodes were swollen and the patient very toxic. The serum tube and broth showed virulent Loeffler bacilli. The second specimen, taken eight days later, proved negative. Neither of these patients were catheterized on either occasion. Of the remainder of this group, from one, Hoffman's bacillus was isolated, and from a case of diphtheria complicating scarlet fever and sepsis a specimen taken by catheter showed diphtheria-like bacilli, which, however, proved not to be diphtheria. All the other cases were negative.

TECHNIC

In the first two groups the female patients were catheterized, 20 or more c.c. of urine being drawn into a sterile centrifuge tube. In the case of males the first part of the urine was discarded and the residue passed into sterile centrifuge tubes through a sterile glass funnel. In one or two instances very young males were catheterized. In three cases only 8 to 12 c.c. of urine was obtained. The centrifugalized sediment was treated as follows:

One c.c. was drawn off by pipet, 0.8 of which was put into 3 to 4 c.c. of ascitic broth and the remaining 0.2 poured over a Loeffler serum tube and incubated. Colonies developing on the tube were examined in the routine way, and if any pellicle developed on the broth, it was stained with Loeffler's methylene blue and examined.

In the third group, although we had every confidence in our technic in producing equally if not more definite results than theirs, it was thought advisable to follow exactly that of the three writers quoted. The patients were catheterized after thorough cleansing of the meatus with mercuric chlorid solution and 35 to 40 c.c. of urine drawn into a sterile container. The centrifugalized sediment with 1 c.c. of the urine was drawn off by pipet and one-half of the quantity allowed to flow over each of two Loeffler plates previously tested with a known strain of Loeffler

bacillus. In addition, in four cases 5 c.c. of the remaining urine was put into 75 c.c. of ascitic broth.

In this group there were eight patients, five of whom were females, five children and three adults. With one exception, they were all cases of clinical diphtheria of a pronounced type; the exception was a case which showed only a markedly congested pharynx from which cultures taken on several different days showed typical diphtheria bacilli. The patients had been ill from three to twelve days and were mostly afebrile at the time of the test. All showed the presence of diphtheria bacilli on culture in the throat.

In three cases there was no growth on the plates after twenty-four hours; in the other five, only colonies of cocci were present, probably staphylococci. The ascitic broth also proved negative.

CONCLUSIONS

The two positive findings in our series may well have been due to accidental contamination at the time of taking the urine, especially as a catheter was not made use of in either case. We conclude, therefore, that diphtheria bacilli may occasionally gain access to the blood and be excreted in the urine in very severe cases of diphtheria with marked ulceration of the mucous membrane of the pharynx and tonsils. This fact is of theoretic interest, but of little practical importance to the physician. Finally, we believe that identification of diphtheria bacilli in the urine should not rest on morphologic characteristics alone, but be confirmed by isolation and animal inoculation controlled by the use of diphtheria antitoxin.

THE AMMONIACAL DIAPER AND ITS CORRECTION

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The occurrence and persistence of a strong ammoniacal odor on an infant's diapers is noted with sufficient frequency to remove it from the categories of rarities. If I mistake not, it has usually been ascribed to decomposition of the urine after its passage. When the odor is detected by the physician inquiries are commonly made as to the length of time since the diaper was removed and injunctions are issued to the mother to see that the diaper is changed promptly when it is wet.

No one of our American text-books deals with this phenomenon, so far as I have been able to determine, or offers suggestions for its correction. It is therefore probable that the condition has not received any general attention. For my own part, I must admit that while I have long been familiar with the ammoniacal diaper, I have only within the last two years understood its etiology or recognized its indications in the dietetics of infancy. While this enlightenment might have come earlier had my search chanced to follow the right channels, the fact that the condition has not found its way into our text-books has led me to think that others may have no solution for this problem, and that it may be admissible to discuss the question and relate several cases in point.

Case A.—Female child. Placed under my care Aug. 25, 1911, when she was 21 months old. For ten days she had had digestive disturbances, loose movements, and fever. Her temperature when first seen was 104 F. As soon as a specimen of urine could be obtained, microscopic examination readily diagnosticated a pyelitis, for which she was immediately placed under treatment. Owing, however, to the frequent bowel movements, daily observations of the diapers were necessary, and it was noticed that they always had a strong ammoniacal odor. This, however, abated under the administration of potassium citrate, which was employed in considerable doses for the cure of the pyelitis.

Paradoxical as it seemed to be that a medication which would cause alkalinity of the urine would also act to reduce the production of ammonia, such appeared to be the case, and, indeed, the mother wrote me later in the fall saying that she had several times attempted to discontinue the potassium citrate, but had been forced to give one or two doses daily because otherwise the ammoniacal odor would return. A

number of sporadic inquiries among medical confrères elicited no satisfactory explanation, and although the matter was constantly in mind, the quest lapsed until the occasion arose for a careful rereading of Keller's monograph on "malt-soup." Here I found what I desired in his introductory recapitulation of his previous work on the ammonia excretion of infants suffering from gastro-intestinal disturbances.

Before discussing this, however, let me add further details of Case A. Her history showed that she was nursed for five months, and was thereafter entirely bottle-fed. The mixture given was more than half top milk, derived from a rich Jersey milk. After having apparently done well on this for two months she began to show mucus in her stools, and develop temperature from time to time. A malt-soup mixture was substituted by the family physician for about two months, and again followed by granum gruel and Jersey milk. At ten months of age she was given undiluted Jersey milk, and was considered to have done fairly well until the series of disturbances extending over several weeks, which culminated in the discovery of her pyelitis. During this latter period the ammoniacal odor of the diapers was noticed. The child had suffered, and still suffers at times, from seborrhoeic eczema. After the disappearance of the ammonia, which was facilitated by the use of a milk less rich in fat, she still had periodical disturbances of digestion of a so-called bilious type, but has recently been free from the latter since the milk given her has been limited to a pint of skimmed milk daily.

CASE B.—Female, native of Ecuador. Referred to me by Dr. Snyder, of Birmingham, Ala. Seen first on Oct. 28, 1912, at the age of 14 months. She had been nursed seven months, and while so nursed was in good condition. Then weaned rapidly and fed on half cow's milk and half gruel. This was followed by indigestion and disturbance of the bowels. A peptogenic milk powder mixture, made up with the usual amount of cream, was then tried. Shortly after, an ammoniacal odor of the diapers was noticed, which had now persisted about three months, although the mixture at present was made up with plain milk, as the cream did not seem to agree. The child weighed 19 pounds and 4 ounces, was pale, restless, slept poorly, and had movements only when assisted. She frequently showed seborrhoeic eczema. The stools were pale, constipated, somewhat large, and often contained mucus.

With a definite reduction in the fat, digestion was better, she slept more, and was less restless and irritable. The ammonia odor tended to disappear, but returned when an effort was made to increase the fat. Final disappearance of the ammonia was doubtless favored by the use of considerable lime water in the food mixtures, and milk of magnesia as a laxative. After several attacks of cough and temperature, which, owing to a house epidemic, were diagnosed as grippe, but in which the temperature usually subsided on clearing the bowels and reducing the fat in the food, skim milk was resorted to, with an increase of other articles in the diet, and the stools for the first time assumed a better color and consistency and were passed without the aid of a suppository. When last seen, April 7, 1913, the child's general condition, color, weight and disposition were much improved, and there had been no return of the ammonia.

CASE C.—Male infant. This child I had seen but once, in September, 1912, when it was thriving and exclusively breast-fed. Thereafter, the parents occasionally sought advice by letter. On Feb. 2, 1913, when the infant was eight

and a half months old, and weighed 19 pounds, 12 ounces, the mother wrote stating that there was a strong ammoniacal odor about the diapers, and inquired whether this was negligible as long as the child gained weight steadily. She also stated that the infant was now getting two supplementary bottles daily, of 7 ounces each, and one complemental feeding of 3 ounces, but the composition of the food was not mentioned. Stools were dull yellow instead of golden color. An older child, having had much difficulty in digesting fat, the mother asked whether the fat might also be at fault in this case.

I at once replied that, although she had omitted informing me of the composition of the artificial feeding, I had no doubt that the ammonia was due to high fat feedings, and that pending the receipt of the formula employed I advised cutting the fat in the mixture down sharply. February 9 (one week later) a second letter informed me that for the past six weeks the infant had been receiving artificial food made from a rich milk, which appeared to be about one-fourth cream. The present formula was:

Whole milk	13 ounces
Gruel	6 ounces
Lime water	1 ounce
Milk sugar	½ ounce

Upon receipt of my letter, 2 ounces of cream had been removed from the top of a *pint* bottle before securing the 12 ounces now used in the formula. Upon the third day after this radical reduction in the fat the ammoniacal odor had temporarily disappeared, diapers worn at night being naturally the last to show improvement. A subsequent but temporary relapse was relieved by removing 6 ounces of cream from a *quart* bottle and increasing the lime water to 4 ounces in a total of 26 ounces of milk mixture.

CASE D.—Male, aged 3 months; weight, 10 pounds, 3½ ounces. Seen March 25, 1913. Was nursed two weeks, then fed on formula of barley water, milk, lime water and milk sugar, which was now at least of fairly appropriate strength. The mother had for some time noticed ammoniacal odor from the diapers, which was most marked after she had yielded to the insistence of her husband and put for some days into each 3½-ounce feeding 1 ounce of gravity cream. Since the child was not thriving, although now on a fairly rational formula, change was made to a malt-soup mixture, with prompt improvement in weight and disappearance of the ammoniacal odor after four days.

CASE E.—Female, seen March 3, 1913. Aged 6 months. Weight, 12 pounds, 10½ ounces. Nursed for two months, during which time she did well, but thereafter variously fed and over-fed. On and off for some time, a strong ammoniacal smell about the diapers. Mother states she had been unable to increase the plain milk above 18 ounces in a 36-ounce formula without disturbance. Some hard curds in stools. Instructions were given to remove 4 ounces of cream from top of quart bottle before taking milk for the feedings; also, to boil the milk, to prevent formation of hard curds; to substitute dextri-maltose for milk sugar. Four ounces of lime water were to be used, and the skimmed milk in the formula gradually increased. April 8: General improvement; stools no longer hard balls, but now once or twice daily; no hard curds. Gain in weight has begun. Ammonia odor decreasing; none noticeable about diaper of previous day, or one freshly removed in office.

These five cases permit the deduction that in infancy a noticeable ammoniacal odor to the diapers may yield either to the administration of alkalies, or to a reduction of the fat in the milk mixture, or to a combination of both measures.

In order to understand the etiology of the presence of ammonia in the urine in excessive quantities, we can do no better than to follow more or less the conclusions of Keller, as contained in his personal writings, as well as in those published in joint authorship with Czerny:

Ammonia does not appear in the urine of normal infants in sufficient quantities to make its presence known by the odor. Such odor is a concomitant of gastro-intestinal disturbance, although it by no means appears in all such cases. Under normal conditions, a considerable portion of the nitrogenous constituents of the food is transformed in the organism into ammonia compounds, and then converted by further chemical processes into urea and excreted as the latter in the urine. A large part of the urea is formed in the liver. Since changes in that organ were commonly found in gastro-intestinal cases, it was at first suggested that these changes might interfere with urea formation, and lead to excretion of larger quantities of ammonia in the urine.

But an increase of ammonia excretion can have another explanation, which depends on the chemical property of ammonia to combine with acids as an alkaline base. While under normal conditions all but a little of the ammonia becomes urea and is excreted as such, if under abnormal conditions there is present in the body an excess of unoxidized acids for whose neutralization the available supply of fixed alkalies does not suffice, the ammonia can then take the place of fixed alkalies and form with the acids ammonia salts, which will be excreted in the urine. As the ammonia salts in the urine increase, the urea is correspondingly decreased, and *vice versa*. Therefore, an increased excretion of ammonia can be caused by an increased production and excretion of acids, except that in cases of fat intolerance the fatty acids formed in the intestines are not often absorbed and oxidized normally, but call for an increased expenditure of alkalies for their neutralization.

The abnormal presence of acids may arise from two sources—either from an increased production during the processes of metabolism, or from either an increased formation or decreased absorption in the intestinal tract. The acids ordinarily formed by metabolic processes are readily oxidized in the body, but some of the abnormal acids may be

oxidized with great difficulty, if at all. This complicates the problem if the acids are present in excess, for if they be not oxidized they must be neutralized either by calling on the fixed alkalies or by calling the ammonia into requisition.

Two important factors, therefore, in determining the amount of the ammonia excretion are the condition of the infant and the type of its food. If the condition of the child is such that the normal power of absorbing acids from the intestines or of oxidizing acids is reduced, then other resources must be brought into play, and in consequence ammonia may more promptly appear in the urine. But it is the type of the food which more commonly plays an important part. Neither proteid nor sugar, despite the possible acid fermentation of the latter, has been shown by experimentation to increase the ammonia excretion when given in the food in excess. It is reserved for the fats to play the sinister rôle through the formation of fatty acids. In gastro-intestinal disturbance the ammount of ammonia excretion may indeed be increased or decreased at will by experimental variations in the quantity of fat given.

Now, were the ability of the organism to produce ammonia unlimited, so that in intestinal cases any amount of acids formed could be fully neutralized, there would be no pathologic effect on metabolism, and we would have no occasion to speak of an acid intoxication. But this is not the case where conditions are such as to produce acids abundantly. Neutralization is not effected solely by the ammonia, but the fixed alkalies are also called on to neutralize the unoxidized acids, and thus alkalies are lost in both the urine and the feces.

We may therefore assume that where in gastro-intestinal cases in infants there is enough ammonia in the urine to reveal itself by its odor, there is also a loss of the fixed alkalies. These are taken from the blood, but since the blood manages to maintain a pretty constant alkalinity, they must eventually be derived from the tissues. Therefore, the less the available alkalies taken into the body, the greater the necessary abstraction of alkali from the tissues.

Our therapy of excessive ammonia excretion is therefore to be directed toward two ends: First, to prevent the improper formation of acids, and second, to prevent undue loss of alkalies. The latter (loss of alkalies) can be partially effected as a first step and further injury to the body averted by the immediate administration of alkalies by the mouth. A rather limited experience leads me to believe that calcium, magnesium

and perhaps potassium are better bases for our alkaline treatment than sodium. But the second and more fundamental and effective measure is to promote a better metabolism of the fats by reducing the amount with which the organism is called on to cope. In short, the food we administer should, if possible, be such as to be fully digested and oxidized with the least formation of acid products.

The fact that in some serious cases of gastro-intestinal disturbance even breast milk is not satisfactorily oxidized, makes the problem of producing suitable artificial feedings for these infants a more difficult one. In the better types of private cases—such as I have related—provided they have not been too long neglected, and especially if there has been a gross error in the amount of fat in the food mixture, administration of alkalies to saponify the excessive fatty acids and the reduction of the fat will often suffice. In hospital and neglected cases of longer standing the powers of absorption are reduced, the condition is more persistent, and unless the continued use of a completely fat-free milk effects a cure and can be made to furnish a sufficient nourishment, we may find it advisable, as did Keller, to employ a malt-soup mixture in which the relatively low fat is compensated by an abundance of readily absorbable carbohydrates.

The conclusion is probably justified that the detection of a noticeably ammoniacal odor on the diapers of an infant, especially if the diaper has been recently removed, and the phenomenon is repeated, points to a definite disturbance of metabolism. Furthermore, this ammoniacal odor may be regarded to some extent as an index of the disturbance, since it tends to disappear when the food has been adjusted so as to allow of more perfect metabolism. For the present, the fat of cow's milk seems to be the more frequent offender when given in excess of the normal capacity, or in cases of fat intolerance when given in excess of the individual's capacity.

More attention should be paid than has been paid in the past to the ammoniacal diaper as a clinical sign. The great desideratum in imparting to others the principles of infant-feeding is to be able to point out definite indications for changes in the composition of the food. An odor of ammonia on the diaper furnishes such indication, for it at once directs attention to a disturbance of metabolism, presumably traceable to an actual or relative overfeeding with the fat of cow's milk.

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DISCUSSION

DR. COWIE: I should like to call attention in this connection to the importance of routine examinations for the acid bodies in infants' urine. The tests are very easily made and when positive the degree of acidosis is very easily determined by the Folin ammonia test. I believe some children die from unrecognized acid intoxication. The occurrence of acetone and diacetic acid in an infant's or child's urine may be of no particular importance; on the other hand, their persistent presence and a high degree of acidosis may lead to serious consequences. Simple measures usually suffice to overcome this intoxication unless it is associated with glycosuria. A collection of cases such as Dr. Southworth has given is of interest particularly if accompanied by quantitative estimations.

DR. SOUTHWORTH: I wish to emphasize the importance of a noticeable ammonia odor in an infant's stools and urine, which involves no elaborate tests. Many are doubtless familiar with this variation of this ammonia quotient in the urine but no one, so far as I know, has called attention to the odor on the diapers of infants as a clinical sign.

DUODENAL ULCERS IN INFANCY

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Until recently, duodenal ulcers have been considered rare in infancy and childhood. Since 1908, groups of cases have been published by several writers, and the increasing number of reports during the past three years indicates that the condition is not a very uncommon one, and that it has been probably overlooked in the past.

In the literature I have found references or full reports of ninety-one cases of duodenal ulcer in the first year of life, making, with four cases of my own reported in this paper, ninety-five cases for study. All but twenty-one of these have been published since 1908. These facts indicate how little this condition was known until five years ago. In the post mortem records of the Babies' Hospital embracing 1,800 autopsies, fully 90 per cent. of which were in children under 1 year, duodenal ulcer is recorded but four times, and, curiously, three of these cases were observed within a period of three months, the other case two and a half years before. It is doubtless true that had it always been carefully looked for, other cases might have been discovered.

Entz[1] (Budapest) reports 10 instances of duodenal ulcer in 364 autopsies on infants under 1 year, made in an infant asylum. Schmidt[2] (Breslau) observed 20 cases in 1,109 autopsies in infants under 1 year. A still greater frequency is indicated by the observations of Helmholz,[3] who found in 16 autopsies on atrophic infants, duodenal ulcers in 8. He calls especial attention to certain superficial ulcers which may easily be missed even when autopsies are made with considerable care, since they cause no symptoms during life, and neither hemorrhage nor perforation is found at autopsy. Half his cases belong to this group. Granting that there is a considerable number of such ulcers which may be detected at

1. Entz: Közhórházi Orvostárs üléski jkoe, Budapest, Nov. 4, 1908, quoted by Flesch in Jahrb. f. Kinderh., lxxvi, 542.

2. Schmidt: Berlin Klin. Wchnschr., 1913, xiii, 593.

3. Helmholz: Deutsch. med. Wchnschr., 1909, p. 534; Arch. Pediat., September, 1909.

autopsy only with some difficulty, even then we cannot assume that duodenal ulcers in infancy are at all common. However, as compared with round peptic ulcers of the stomach they are certainly much more often seen. Thus Entz observed ten duodenal to one gastric ulcer. There is no case of peptic ulcer of the stomach in the autopsy records of the Babies' Hospital.

Of sixty-five cases in which the age of infants with duodenal ulcers is given, 70 per cent. of the patients were between 6 weeks and 5 months old, the greatest frequency being between the sixth and tenth week; only seven patients were over 5 months old; nine were in the new-born. The age incidence is very striking. It corresponds very closely with the age incidence of deaths from marasmus.

While duodenal ulcers may be seen in patients of any age and in those who are well nourished, the great majority occur in infants of the marasmus (atrophic) type. Whether there is a more definite association than simply a lowered vitality of the mucous membrane of this part of the intestine, it is impossible to say.

Two predisposing factors seem of some importance: A lowered general vitality of the patient, as in infants suffering from marasmus, and previous digestive disturbance, a history of which is present in a very large proportion of the cases.

The situation of the ulcer in the great majority of the cases is in the posterior wall of the duodenum. Practically all of them are above the papilla, and when but a single ulcer is present the usual seat is just below the pyloric ring (Fig. 2).

Of 51 cases in which the point is mentioned, there was only a single ulcer in 35 cases; two ulcers in 8 cases, and more than two in 8 cases. In size the ulcers vary from 2 or 3 mm. to 1.5 cm. in diameter. Duodenal ulcers are circular in shape, they have shelving, sharp edges, usually described as "punched out," and often show at the base open blood-vessels of considerable size. They may involve only the mucous membrane or they may go to the muscular coat, quite to the peritoneal coat or may perforate.

Microscopical examination shows an almost complete absence of round celled infiltration and other evidences of inflammatory reaction. The mucous membrane of the duodenum elsewhere is generally normal, except that it may be blood stained. Large clots may be present in the duodenum or the small intestine lower down and blood may even be found in the colon. The stomach also may contain fresh or old blood. It is

rather surprising that although gastric ulcers are believed to have the same etiology and pathology, in but a single case have I found recorded the coexistence of gastric and duodenal ulcers in the same patient, even including the cases observed in the new-born.

The association of duodenal ulcer with burns is so constantly mentioned in works on adult medicine that it is of some interest to note that not one of the recorded cases of duodenal ulcer in infants which I have collected have complicated burns. Ulcer has been found complicating many pathological conditions, but there seems to be no adequate reason for connecting it with any except marasmus, and even this is regarded by some writers as accidental.

I have nothing to add to the generally accepted view of the pathogenesis of these ulcers, viz., that they are due to thrombosis followed by self digestion of the mucous membrane over a circumscribed area. The situation of the ulcers, above the papilla, indicates that the lesion is due to the action of the gastric juice.

Below the papilla the presence of the alkaline pancreatic and hepatic secretions seems to exert a protective influence on the mucous membrane of the intestine. That it is the direct action on the intestine of the gastric juice not yet neutralized is indicated by an observation of Freund's[4] on an infant 2 months old, who was operated on by gastro-enterostomy for pyloric stenosis. For a time progress was favorable, then bloody stools followed by death, the autopsy showing ulceration of the jejunum below the opening which communicated with the stomach.

SYMPTOMS

In a little more than one-third of the recorded cases no symptoms which could be attributed to ulcer were present during life, the condition being found at autopsy in infants dying of intercurrent disease or of marasmus.

In a second group of cases death occurred suddenly in collapse, sometimes preceded by ordinary gastro-intestinal symptoms and sometimes not. In a few patients with such a history the autopsy disclosed a concealed hemorrhage, the duodenum, and in some cases the intestine lower down, containing large clots, though no bloody discharges were present during life. In other cases there was found an acute perforating ulcer and usually commencing general peritonitis. After the development of

4. Freund: Mitt. a. d. grenzgeb. d. Med. u. Chir., xi, 326.

the first symptoms of collapse death may ensue in a few hours, or life may be prolonged for a day or a day and a half, rarely longer in patients of this age and class. The diagnosis of peritonitis under these conditions is extremely difficult, since neither vomiting, fever nor distention may be present, the only thing suggesting it being the acute collapse. On account of the age of the patients such symptoms as pain and localized tenderness, of much value in older subjects, are of no assistance in making the diagnosis in infants.

There is then practically only one definite symptom pointing to duodenal ulcer, viz., hemorrhage. This may appear as blood vomited or as blood in the intestinal discharges. Some idea of the relative frequency with which these symptoms occur may be gained from the following statistics: Of 64 cases of duodenal ulcer in which the clinical histories are recorded, bloody stools were noted in 28; bloody vomitus in 10; both bloody stools and bloody vomitus in 6 cases, 4 of these being in the new-born. In 2 patients there was no discharge of blood during life though the intestine at autopsy contained large blood-clots. The blood vomited may be bright, clear blood, or coffee-ground material. It is not usually in large amount, although in the new-born as much as half an ounce or an ounce has been recorded. Blood from the bowel may be in such small amount as merely to show a trace in the stool, or large clots may be passed and even fluid blood in considerable quantity. Once the hemorrhage has occurred it is apt to persist until the death of the patient, which usually comes within twenty-four or thirty-six hours from its first appearance. It is surprising how small an actual loss of blood may produce very serious symptoms in the class of patients in which most of these ulcers occur. In several cases the collapse has been so acute and so severe as to suggest perforation, though the autopsy showed only concealed intestinal hemorrhage. It is, then, the appearance of blood in the stools, usually in considerable amount, which first suggests duodenal ulcer, and in patients of the marasmus class or in young infants from 1 to 5 months old this cause of hemorrhage should always be borne in mind.

The association of duodenal ulcer with spasm of the pylorus has been too often observed to be considered accidental. In Torday's case,[5] an infant 8 months old, exhibited characteristic symptoms of pyloric stenosis — persistent, forcible vomiting and marked peristaltic waves — yet the

5. Torday: Jahrb. f. Kinderh., 1906, lxiii, 563.

autopsy showed no stenosis, but a duodenal ulcer just below the pyloric ring, with a greatly distended stomach. Ulcer of the duodenum associated with pyloric stenosis has been mentioned by Finny,[6] Ibrahim[7] and Freund,[4] and Birk[8] observed three cases associated with pyloric stenosis and one with pyloric spasm. In the above references the distinction between pylorospasm and pyloric stenosis is not always clearly made. It is easy to see how an ulcer in the duodenum just below the pyloric ring might by irritation cause pyloric spasm with symptoms closely simulating pyloric stenosis, although the latter condition was not present. It is perhaps enough in this connection to call attention to the association of these two conditions, and to emphasize the point that when symptoms suggesting pyloric stenosis are seen for the first time in an infant over 3 or 4 months old, duodenal ulcer should be borne in mind as a possible explanation.

Something should also be said regarding the relation of duodenal ulcer to melena, or the gastro-intestinal hemorrhages of the new-born. Dusser,[9] in thirty-one collected autopsies on such cases, mentions five in which the only lesion was a single duodenal ulcer; in four of these, blood was vomited as well as expelled by stool. In a patient of my own (Case 4) dying on the twelfth day, multiple erosions were found in the stomach as well as an ulcer in the duodenum. In reviewing the cases seen in the new-born one is struck by the fact that the hemorrhages were more extensive than in other cases of duodenal ulcer and seemingly out of proportion to the size of the ulcer; also that they were usually both gastric and intestinal. This gives rise to a suspicion that the cause of the bleeding in these cases is a general one and not entirely the ulcer and possibly not even connected with it. There are no sufficient reasons for invoking a different pathology for the ulcers occurring at this time of life and those which are seen in later infancy.

In only one case, No. 2, of my own series, was jaundice mentioned as an associated symptom. In this case the connection was not quite clear. The jaundice was so intense as to suggest malformation of the bile ducts, yet no obstruction was found at autopsy either in the cystic or hepatic ducts. It was apparently due solely to catarrhal swelling of the mucous membrane of the ducts.

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6. Finny: Proc. Roy. Soc. Med., 1908-9.
7. Ibrahim: München. Ergeb. der inn. Med. u. Kinderh., 1908, i, 220.
8. Birk: Referred to by Helmholz, Arch. Pediat., September, 1909.
9. Dusser: Thèse, Paris, 1889.

DIAGNOSIS

The gastro-intestinal symptoms preceding duodenal hemorrhage are usually of a mild type and subacute, so that enterocolitis with its frequent bloody and mucous stools is not likely to be confounded with ulcer. There is lacking also the persistent vomiting (not bloody), the paroxysmal pain, the tenesmus, with the passage of blood and mucus from the bowels, but no fecal matter, all of which are characteristic of intussusception; although the age of the patients, the suddenness of the invasion and the acute prostration somewhat suggest it. With blood appearing both in the vomitus and in the stool one might be in doubt as to whether the lesion was gastric or duodenal. The far greater frequency of duodenal ulcers of course makes this lesion much the more probable one.

In the case of symptoms pointing to acute perforative peritonitis in an infant, duodenal ulcer should be remembered as one of the possible causes and next to appendicitis probably the most frequent one.

From what has been said it will be evident that the diagnosis always has been and still is a matter of much difficulty, and it is not surprising that the disease has been recognized only at autopsy in the great majority of the cases reported. There is one method of diagnosis which I believe is likely to assist materially in these very obscure cases—the passage of the duodenal catheter. An opportunity to try it was afforded in one of my cases (Case 2). Ulcer was not at first suspected in this patient, but on account of the intense jaundice Hess's duodenal catheter was introduced to see if the presence of bile in the intestine could be demonstrated. On its withdrawal the catheter was found to contain a clot of blood, but no bile. Although the duodenal catheter had been passed many times before in other patients, blood had never been seen under such circumstances. We did not, therefore, believe it could be the result of traumatism. The suspicion of duodenal ulcer was strengthened by the presence of blood in the stools. Given a young infant with intestinal hemorrhage and showing no other symptoms of colitis, intussusception, polypus, etc., the introduction of the duodenal catheter is not only justified, but indicated, and it may give, as in my own case, very definite information on which in the future successful treatment may possibly be based. I know of no other means of diagnosis which will tell as much. The possibility of doing harm by the catheter cannot be denied; but the risk in my opinion is so slight that it may be ignored.

PROGNOSIS

In a condition so difficult of diagnosis and where the great majority of the cases are recognized only at autopsy, there are but few data available for prognosis. That such cases may recover seems certain from the observation of Schmidt, who found at autopsy in an infant dying of some acute infection at 5 months the cicatrix of an old ulcer, and also from one of Helmholz's cases in which recovery followed after an attack with fairly typical symptoms. The probabilities are that such a termination is a very infrequent one. The fatal outcome is due quite as much to the condition of the patients in which most of the ulcers are seen as to the ulcer itself.

TREATMENT

Regarding treatment, little can be said; medical treatment is to be symptomatic only, and surgical treatment is as yet inadvisable in most cases.

REPORT OF PERSONAL CASES

CASE 1.—*Perforating duodenal ulcer followed by general peritonitis.*

History.—D. M., a female child, 3 months old, admitted to Babies' Hospital because of loss of weight, vomiting and constipation. Family history unimportant; ninth child; plump at birth; no breast feeding, and had never thriven. The previous history suggested pyloric stenosis; there had been frequent vomiting since the child was 2 weeks old. This occurred after nearly every feeding and was forcible, but the food had been principally milk formulas rather high in fat. Examination showed a poorly nourished infant of the marasmic type: weight but 5 pounds, 7 ounces. Except for the presence of a moderate degree of thrush and erythema of the buttocks, the physical examination was negative. The abdomen was normal; there were no peristaltic waves and no pyloric tumor; heart and lungs normal.

The infant was placed on a skimmed milk formula containing fat 0.60; sugar 6.00; protein, 1.20 per cent. The child lived eight days after admission, during which time she vomited in all but six times, twice on the first day, twice on the second day and only twice thereafter. The vomiting was not forcible. The appetite was good; the child generally took her food well. The bowels moved usually twice a day; for the first three days the stools were yellow, smooth and well digested; afterwards they were yellow and thin, but never frequent, and no blood was present. Even from the beginning the prostration was marked. The temperature was habitually subnormal in spite of artificial heat and the use of a cotton jacket. The loss in weight continued for the first four days, after which the child became somewhat edematous. During the last three days in the hospital the temperature was not above 95 F. Death occurred quite unexpectedly in a condition of collapse. There was no marked abdominal distention and no tenderness was noted.

Necropsy.—Permission to examine the brain was not obtained. The heart and lungs showed nothing of importance. On opening the abdominal cavity the parietal peritoneum and omentum were found much congested and showed

numerous small hemorrhages. The peritoneal cavity contained about 70 c.c. of turbid yellow fluid, which after standing deposited a heavy precipitate of pus cells. The cause of the peritonitis was found to be a perforating duodenal ulcer. It was situated on the posterior wall just below the pylorus. It was circular, about 5 mm. in diameter and had a typical "punched out" appearance. No signs of repair at its borders. The mucous membrane of the intestine was blood-stained, but no other lesions were present. The stomach was congested but showed no ulcers. Cultures from the peritoneal fluid showed the streptococcus and colon bacillus. Streptococci were also obtained from the heart's blood and lungs.

Microscopical examination of the ulcer was made by Dr. Martha Wollstein, pathologist to the hospital. There was no inflammatory reaction, but a loss of substance which at one point involved all the coats of the intestine. The edges of the gap were sloping, not undermined. The walls of the mucosa, submucosa and muscular coats forming the edge of the ulcer had undergone necrosis and were converted into a granular, poorly staining layer. The epithelial layer of the mucosa was degenerated or absent for some distance beyond the borders of the ulcer; beyond this the duodenal wall was normal. The adherent pancreas was also normal.

CASE 2.—*Two ulcers in the duodenum; intense jaundice; intestinal hemorrhage; death from marasmus.*

History.—M. N., a male Italian child, 2 months old, was admitted to the hospital on account of marked jaundice and progressive loss of weight. The parents were not very intelligent and no detailed previous history could be obtained. It was ascertained, however, that the child was born at full term after a normal labor and had been breast fed up to admission. It had never thrived. Jaundice was first observed two weeks before and had steadily increased. The stools were gray and the urine stained the napkins. The history of the jaundice, given by the parents, was corroborated by a physician who had previously seen the patient.

Examination on admission showed a small, wretched looking infant; weight 5½ pounds. The jaundice was intense, the skin being of an olive-green hue. The sclerae and mucous membranes were also stained with bile. Nothing of importance was discovered in the head, neck or chest. The abdomen was tympanitic, only moderately distended, the circumference being 13½ inches. The lower border of the liver was felt just below the costal margin; the spleen was not palpable. No abnormal masses were felt.

The child was placed on a milk formula having the following percentages: Fat, 0.60; sugar, 5.00; protein, 1.20 per cent. This patient also lived eight days after entrance into the hospital. During this time the temperature was much of the time subnormal, 94 F. being noted on one occasion. The urine gave a strong reaction to bile, but contained no blood or casts; urobilinogen test negative. All the stools were white, pasty, offensive and large for the food taken. The presence of bile salts could not be demonstrated. The stools contained immense quantities of fat which formed approximately 90 per cent. of the dried residue. This was chiefly in the form of soaps, although there was also a large excess of neutral fat. There was both macroscopic and occult blood in the stools. At no time was there diarrhea, and there was no vomiting of blood. Both Wassermann and tuberculin tests were negative. Blood examination at the time of admission showed: Hemoglobin, 55 per cent.; red cells, 3,900,000; white blood-

cells, 15,000; polymorphonuclears, 23.3 per cent.; lymphocytes, 76.3 per cent.; eosinophils, 0.3 per cent. One week later the hemoglobin was but 20 per cent. and red cells, 1,700,000.

The duodenal catheter was passed without much difficulty to ascertain the presence of bile. None could be obtained but on withdrawing the tube it was found to contain a blood-clot. This was repeated three or four days later and a larger clot obtained. The child grew progressively worse and died of exhaus-

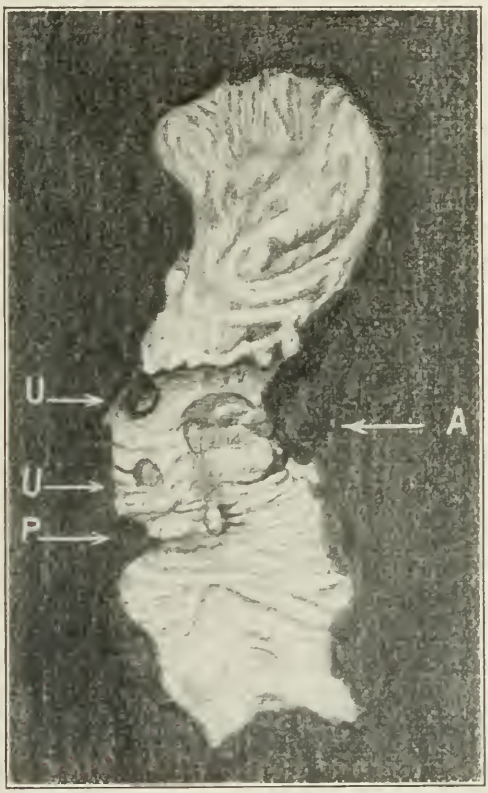

Fig. 1.—Two ulcers in the duodenum. Case 2. A, artefact; U, ulcers; P, papilla.

tion. From the presence of blood in the stools and in the duodenal catheter the diagnosis of duodenal ulcer was made.

Necropsy.—Body emaciated and deeply jaundiced, and all the internal organs deeply bile stained; a small area of bronchopneumonia in right upper lobe; heart normal; pancreas and peritoneum normal; spleen, normal in size and appearance. Liver, dark greenish color, not enlarged and not hard; capsule thickened, especially at the border; slight increase in the connective tissue; no recent exudate;

gall-bladder contained thick, dark green bile which could easily be expressed through the duct into the duodenum. Cystic and hepatic ducts appeared normal. Duodenum showed two small round "punched-out" ulcers, each about 5 mm. in diameter. One was situated just below the pylorus (Fig. 1). It extended quite to the peritoneal coat; at its margin was seen a small blood-clot from a bleeding vessel; a large blood-clot in the duodenum lower down. The other was similar in appearance and situated 1 cm. lower down in the duodenum. The rest of the intestine, both small and large, showed areas of congestion and enlargement of the solitary follicles. The kidneys were normal, except jaundiced. Cultures from the lung showed Gram-negative bacilli and pneumococci.

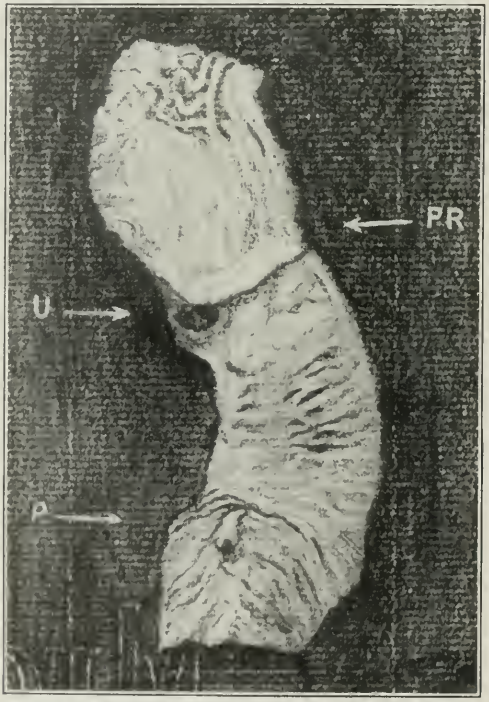

Fig. 2.—A single ulcer of the duodenum in the usual situation. Case 3. U, ulcer; P, papilla; P. R., pyloric ring.

Microscopical examination by Dr. Wollstein showed a loss of epithelium of the mucosa, edema of the mucosa and submucosa, but no cellular infiltration. The muscular and peritoneal coats were normal. The liver showed no increase of connective tissue. The blood vessels and capillary bile ducts were normal.

CASE 3.—*Single ulcer of the duodenum; concealed hemorrhage; sudden death.*

History.—M. F., a female child, 4 months old, admitted to hospital on account of diarrhea and vomiting which had lasted one week. Family history unimportant. For the first two months the baby had been breast fed and did well; then had been put out to board and had not thriven. The bowels had been generally

loose, but no vomiting had been noted till one week before admission. Stools thin and green, four or five daily; no fever, but steady loss in weight.

On admission the child weighed 8 pounds, 14 ounces; fairly well developed; did not appear acutely ill; heart and lungs normal; spleen palpable one-half inch below costal margin; liver, enlarged, the lower border 1½ inches below the costal margin; Wassermann negative. Blood: hemoglobin, 60 per cent.; red cells, 4,400,000; white cells, 14,000; polymorphonuclears, 40 per cent.; lymphocytes, 60 per cent.

The child was put on protein milk (*Eiweissmilch*) 4 ounces every three hours. No further vomiting occurred after admission. The stools continued from four to six a day and for the most part were thin and of a grass green color; no macroscopic blood. The temperature remained normal for four days when it rose to 101.4 F., later to 102.6 F. Until this day the child did not appear seriously ill and looked much the same as during the previous four days. A marked pallor was then noted, the patient looking almost exsanguinated, though no blood was seen in the stools and no other hemorrhage had been observed. Death occurred quite suddenly on this day, almost without warning.

Necropsy.—Body well nourished; small areas of atalectasis in lungs but no pneumonia; liver extremely fatty, with a few small subcapsular hemorrhages especially on the under surface. The stomach contained a large amount of blood-stained fluid and showed many submucous hemorrhages, but no ulcers. The stomach contained one large soft, dark red clot which extended into the duodenum. Three millimeters below the pyloric valve on posterior wall (Fig. 2), there was an oval ulcer, 4 by 8 mm., edges sharply defined; no surrounding inflammation. At the base of the ulcer small clots and a bleeding point were discovered. The ulcer had the typical "punched-out" appearance; it extended through the muscular coat to the peritoneum. Mucous membrane in the neighborhood was pale. The rest of the small intestine showed nothing abnormal. Nothing of importance in the other viscera.

Microscopical Examination by Dr. Wollstein: The normal mucosa showed an abrupt solution of continuity without any inflammatory products. The epithelial layer and Brunner's glands had disappeared leaving an irregular, narrow, glandular, poorly staining layer internal to the muscularis mucosa. The submucosa contained no Brunner's glands, but showed no inflammatory products. The muscular coats were normal. The duodenum on either side of the ulcer was quite normal, even the epithelial covering being intact.

CASE 4.—*A single ulcer of the duodenum, with multiple erosions in the mucous membrane of the stomach in a newly born child; no hemorrhages present.*

History.—R. D., a male child, 12 days old, was admitted for vomiting and diarrhea which had existed almost from birth. The infant was one of twelve, five of whom were living and six dead; all from marasmus, the history stated. The birth was at term and the labor normal. No breast feeding had been given; at first the food had been condensed milk, afterwards nothing but barley water. All the food had been poorly taken and much of it had to be forced. The stools had never been normal; for a few days before admission they had been from two to five daily, thin, of a yellow-green color and contained mucus. Vomiting had occurred after almost every feeding. The stomach was emptied two and a half hours after feeding and was found to contain a small amount of mucus, but no blood.

On admission the child was in extremely bad condition, very feeble, almost moribund in fact; weight six pounds. No local evidences of disease in the

abdomen; râles at the bases of both lungs; no nervous symptoms; temperature nomal.

The child was put on a weak milk formula, fat 0.90; sugar, 5.00; protein, 0.70 per cent., and castor oil was administered. On the following day the temperature rose to 104.6 F. and remained above 102 F. the entire day. Vomiting continued, though but little food was taken. The stools never contained blood but were frequent, thin and green, at times only a stain on the napkin. There was no improvement in any of the symptoms and death occurred forty-eight hours after admission.

Necropsy.—Body wasted; nothing of importance in thoracic organs; liver, fatty and slightly congested, no increase in connective tissue; pancreas congested; kidneys showed uric acid infarcts in many pyramids.

The stomach contained blood-stained mucus and the mucous membrane showed many erosions extending quite to the muscular coat. They were of irregular shape, some rounded and some elongated. They were below the rugae rather than on them. In the duodenum was an ulcer 4 by 8 mm. situated on the anterior wall, about 1 cm. below the pylorus and 1 cm. above the papilla. It had a bile stained base; edges congested and elevated. Elsewhere the duodenum appeared normal. The rest of the small intestine showed intense congestion, but no hemorrhages and no ulceration. The solitary follicles of the colon were generally swollen. There was swelling and congestion of the mesenteric lymph-nodes.

I wish to acknowledge my indebtedness to Dr. Stafford McLean for assistance in collecting the literature and to Dr. E. A. Morgan for the drawings of the pathological specimens.

SUMMARY OF LITERATURE ON DUODENAL ULCERS IN INFANCY

The earliest cases reported in the new-born were collected by Dusser[9] in 1889. In thirty-one collected autopsies on gastro-intestinal hemorrhage in the new-born there were five in which duodenal ulcer was found. These are as follows:

Spiegelberg:[10] Case 1. On the fourth day, suddenly, hemorrhage from the stomach and intestine; death in a few hours. Stomach showed ecchymoses only. The duodenum showed round ulcer close under the pyloric valve; swelling in the follicles of the large intestine; no other lesion. Case 2. Thirty hours after birth sudden occurrence of bloody vomiting and shortly afterwards bloody stools; death in twenty-four hours. The stomach contained 30 c.c. of fresh blood; the mucous membrane was normal. Midway between pylorus and papilla a large coagulum in the duodenum; in the posterior wall one large and two smaller ulcers.

Landau:[11] An infant dying on the fifth day had bloody vomiting and bloody stools. Necropsy: Large clots in the stomach; mucous membrane normal. Round ulcer in the duodenum 5 cm. from the pylorus, size 5 by 8 mm. Rest of the intestine and mucous membrane normal.

Kling:[12] Death on the fourth day. Symptoms, vomiting of blood and bloody stools. In second portion of duodenum, posterior wall, ulcer, 1 by 1.5 cm., perforated at one point.

Zeischwitz:[13] Thirty hours after birth copious hemorrhage from the rectum; arterial blood. Death the following morning. In the posterior wall of the

10. Spiegelberg: Jahrb. f. Kinderh., 1869, p. 333.
11. Landau: Ueber Melena Neugeborenen, Monograph, Breslau, 1874.
12. Kling: Ueber Melena Neonatorum, Inaugural Dissertation, München, 1875.
13. Zeischwitz: Schmidt, 1888, xxxv.

duodenum a little above the papilla an ulcer going to the muscular coat; an artery opened; intestines elsewhere normal.

More recently Gruber in a report of seventeen cases under 10 years old, mentioned two duodenal ulcers in the new-born.

Schmidt[2] reports one case in an infant five days old, and one of my own cases, an infant 12 days old, should probably be included in this group.

The principal reports of cases of duodenal ulcers in later infancy are the following:

Veit:[14] An infant 1 week old, previously healthy; sudden onset, pain, fever, anorexia; death in thirty-six hours; no blood in stools or vomitus. Necropsy: coffee-ground material in stomach and intestines; large blood-clot in the duodenum; two duodenal ulcers on posterior wall; no perforation.

Adriance:[15] An infant 10 months old suffering from marasmus with marked gastro-intestinal symptoms for two weeks. Vomiting persistent, but vomitus contained no blood. Four days before death blood from the rectum following intestinal irrigation. After this two or three bloody stools daily until death. Necropsy: bright and dark blood in stomach; a duodenal ulcer, 1 by 2 cm., just below pylorus on posterior wall, going through all the intestinal coats.

Borland:[16] An infant 8 months old; severe general pustular eczema; gastro-intestinal symptoms for three days; vomiting of blood; no mention of blood in stools. Necropsy: round ulcer just below pylorus on posterior wall; large mass of clotted blood in peritoneum; no peritonitis.

Torday:[5] An infant 8 months old, admitted for atrophy and rickets; shortly after began to vomit in a manner characteristic of pyloric stenosis. This continued in spite of diet changes, stomach washing, etc. No blood in the vomitus or stools. Peristaltic waves present. Pylorus, not palpable. Death six weeks later. Necropsy: stomach greatly dilated; no pyloric stenosis; but ulcer 5 mm. below pylorus; blood in the intestines. Author believes that pyloric spasm was caused by the ulcer.

Entz,[1] quoted by Flesch: In 364 autopsies on infants under 1 year, ten duodenal ulcers and one gastric ulcer; ages between 6 weeks and 5 months. Two perforated and caused a purulent peritonitis. Death in three from hemorrhage. In most cases definite gastro-intestinal symptoms with infantile atrophy preceded. Diagnosis usually made at autopsy only.

Küttner:[17] Patient 1 month old; seven days after birth vomiting, diarrhea and for two days bloody stools. Twenty-three days later vomiting of blood and death. Necropsy: A single round ulcer upper part of duodenum, 5 mm. in diameter. Author reports also a case in a child 4 years old. Refers to Collin's monograph[18] who in 279 cases of duodenal ulcer found seventeen under one year.

Finny:[6] An infant, 2½ months old, had been vomiting almost from birth in spite of stomach washing, etc. Pyloric stenosis diagnosed; later bloody stools led to a suspicion of duodenal ulcer, confirmed by autopsy. Two ulcers present 1.5 cm. below pylorus in posterior wall; one had perforated; pylorus contracted and its muscular coat thickened.

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14. Veit: Deutsch. med. Wchnschr., 1881, p. 681.
15. Adriance: Arch. Pediat., 1901, p. 277.
16. Borland: Lancet, London, 1903, ii, 1084.
17. Küttner: Berlin Klin. Wchnschr., 1908, xlv, 2009.
18. Collin: Thèse, Paris, 1890.

Sochaczewski:[19] An infant 5 months old; gastro-intestinal symptoms since 4 weeks old; general condition wretched. During the last twenty-four hours three to four large bloody stools; no vomiting. Necropsy: single ulcer in posterior wall two fingers' breadth below pylorus. Peyer's patches swollen but no other ulcerations.

Helmholz[3] (first communication 1909): Reports nine cases of duodenal ulcer of which eight came to autopsy. Five of these were between three and five weeks old; three between 2½ and 4 months. All were in atrophic children. A single ulcer was present in four of the eight cases. Intestinal hemorrhage was noted in four; in four others no definite local symptoms. In the child who recovered the diagnosis rested on the sudden development of marked prostration; almost collapse, followed by intestinal hemorrhage which lasted three days. Patient was an infant 2 months old and was well five months later. In a second communication (1909), he reports seven additional cases; like the former ones these were seen in different German clinics; all of these patients were likewise atrophic infants. In three intestinal hemorrhage occurred and in one of these there was also perforation; in four there were no definite symptoms. Six of these patients were between 1 and 3 months old and one was 7 months. In three of the cases a single ulcer was present; in four two or more.

Griffith:[20] An infant 6 months old; symptoms for two days; vomiting followed shortly after by trace of blood in the stools. On the following day vomited clear blood several times and one large hemorrhage from the bowel; death in collapse. Necropsy: ulcer, 5 mm. in diameter, in posterior wall of duodenum just below the pylorus. Ulcer extended through the intestine, but adhesions prevented the escape of fluid into peritoneum. Stomach contained 1 ounce of bloody fluid.

Hertz:[21] An infant 2½ months old, artificially fed. Frequent bloody stools for two days, followed by death. A single ulcer in the upper part of the duodenum, 1.5 by .75 cm. in diameter.

Gruber:[22] In 4,208 autopsies, 1,147 peptic erosions, scars or ulcers; 17 duodenal ulcers in children under 10 years; six in infants between 3 and 8 weeks; details not given.

Weill[23] and Gardére: An infant 1 month old; digestive disturbances from birth with diarrhea and irregular vomiting; traces of blood noted in stools, but no real bleeding. Case regarded as a delayed hemorrhage in the new-born, due to intestinal lesion. Necropsy: a single ulcer just below pylorus; blood-clot in the duodenum.

Flesch:[24] An infant, 3 months old, atrophic, anemic, losing weight. Symptoms for last fifteen hours; large, bloody stools; subnormal temperature; death in collapse. Necropsy: two ulcers, one just below pylorus and one just above papilla; follicular gastro-enteritis present.

Schmidt:[2] In 1,109 necropsies on infants in the first year, twenty cases of duodenal ulcer. Most of the patients in poor general condition; ten were atrophic.

19. Sochaczewski: Arch. der Kinderkr., 1909, l, 25.
20. Griffith: New York Med. Jour., Sept. 16, 1911.
21. Hertz: Referat im Hospitalstidende, 1911, liv, 35.
22. Gruber: Referat im München. med. Wchnschr., 1911, lviii, 1668.
23. Weill and Gardére: Lyon méd., 1911, cxvii, 1177.
24. Flesch: Jahrb. f. Kinderh., 1912, lxxvi, 542.
25. Fischl: Pfaundler and Schlossmann, Am. Ed., 1908, iii, 149.

They were seen associated with a great variety of conditions — rickets, whooping-cough, nephritis, empyema, meningitis, pyloric stenosis. Author thinks no closer association with atrophy than with any other condition of marasmus. Of the twenty cases, peritonitis was present in three and hemorrhage in seven. In ten, ulcers were latent. The usual situation was just below the pyloric ring.

Birk[8] (quoted by Helmholz, unpublished): Eight cases; ages eight weeks to ten months. Three with pyloric stenosis; one with pylorospasm; two in normal infants who were well up to a day or two before death from hemorrhage; two with acute pneumoccoccus infections.

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DISCUSSION

DR. CHURCHILL: Dr. Holt spoke of passing a duodenal catheter without apparent injury to the duodenal ulcer. There has been, of course, no injury or perforation in the case where he used the catheter. I would like to ask if he would consider it safe to pass the duodenal catheter in cases suspected to be cases of duodenal ulcer? In gastric ulcers it is considered extremely risky.

DR. GRIFFITH: Some of you perhaps remember that two years ago I reported before this society two cases of duodenal ulcer in children. One of these patients, an older child, did not die and the diagnosis, therefore, lacks anatomical confirmation, although clinically reasonably certain. The other case, a child of 5½ months, came to autopsy, and a single, "punched-out" ulcer, having the ordinary characteristics of the peptic ulcer, was found. This had perforated, causing death from hemorrhage and from peritonitis. I made incidentally a fairly extensive search through medical literature, although by no means a complete one, and referred in my report to many of the cases mentioned by Dr. Holt. Very little, however, was to be found in the different text-books consulted; no reference whatever being made except in a single instance: viz., in the article by Fischl in Pfaundler and Schlossmann's *Handbuch*, where it is said that duodenal ulcer in children is of great rarity. Nearly all the articles on the subject found in journal-literature spoke of the condition as uncommon, with the exception of the thesis of Collins which referred to forty-two collected cases under 10 years of age. Helmholz reported nine cases in atrophic infants and Moynihan referred to cases of melena in the new-born believed to depend on duodenal ulcer. It seems very probable, however, that many of the cases of ulcer, often multiple, found in atrophic infants may be little more than slight erosions and are hardly of the class of the deep ulcer under consideration, which is analogous to that found in the stomach.

Probably duodenal ulcer is more common than supposed, especially in the new-born, and is often overlooked at autopsies. I doubt, however, whether at any period of life it can be called frequent; and beyond the early weeks it is certainly rare.

DR. PISEK: From my own observations gastric ulcer is, as Dr. Holt says, exceedingly rare. In regard to the question he raises as to whether the condition is the result of thrombosis, I should like to cite the case of an infant that came under my notice. The infant was a strong, nursing baby, who had had pneumonia several weeks previously, but had entirely recovered. Symptoms of shock suddenly appeared and I was called in consultation, but by the time I arrived the child had died. We obtained an autopsy on the body which was made a few hours after death. I had expressed the opinion that the child had a duodenal ulcer because of the shock, the vomited blood and blood in the

stool. The autopsy, however, showed a typical gastric ulcer, which in this child we concluded was caused by thrombosis.

DR. LADD: Roentgenograms have been used successfully in adults and I do not see why the Roentgen ray could not be used just as successfully with children to diagnose duodenal ulcers. I would suggest the use of the bismuth meal and the Roentgen ray as a diagnostic aid in these cases.

DR. GRAHAM: In Philadelphia I had a case of an infant six or seven months old which was suddenly taken violently ill and went into collapse and died soon afterwards. The illness had been of such a short duration that the case was referred to the coroner, and I freely confess that before the autopsy I was entirely in doubt as to the cause of death. The autopsy showed a perforating gastric ulcer.

DR. MCCLANAHAN: I merely want to mention one case of duodenal ulcer in an infant aged six weeks, and add a case to the literature of the subject. I am free to confess that diagnosis was not made during life. The infant was not thriving well and finally died very suddenly from profuse hemorrhage from the bowels. The post mortem revealed such an ulcer as described. The child died in a state of collapse.

DR. NICOLL: It is a sad commentary on the thoroughness of the work of those of us who have spent so many years, in the aggregate, in performing autopsies on infants and children that we have so rarely met with duodenal ulcers. I should like to ask Dr. Holt if in his opinion this is due to our lack of careful search, or to the readiness with which such ulcers are overlooked?

DR. HOLT: To begin with, the last question first, I will say this: Large ulcers are seldom overlooked by any one. The kind of cases that might be overlooked by an ordinary autopsy are small, superficial erosions involving the mucous membrane only. The risk of producing a duodenal ulcer by the passage of the duodenal catheter is, I believe, very small. When an ulcer is present, it is usually so well protected, being just below the pyloric ring, that the danger of causing perforation by the catheter is also a negligible one.

CASEIN IN INFANT FEEDING. EXPERIMENTS IN EXACT PERCENTAGES *

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The proteins of cow's milk have been the source of much interesting discussion and controversy among pediatricians. Theories as to their digestibility are changing almost yearly. Whey proteins advocated by Rotch have given place to the "whole proteins" of Czerny, Keller and Walls (which bring forward the digestibility of skim-milk); while others have heated, peptonized and lately precipitated the proteins in further attempts to improve our knowledge and treatment. Up to the present the proteins of milk formulas have not received the attention we should expect. Protein requirements have painstakingly been estimated and the formulas prescribed, but no one has seriously questioned the accuracy of such mixtures. Several days during the summer of 1912, formulas made according to Finklestein's method were found on examination to contain proteins varying from 2.5 to 4.5 per cent. This instance of error led us to investigate the composition of home modifications and laboratory milk formulas.

METHODS OF ANALYSIS

1. *Total Protein.*—Total nitrogen was determined by Folin's modification of Kjeldahl's method. Total nitrogen multiplied by 6.37 gave the total protein.

2. *Casein.*—Casein was determined by the volumetric method devised by Van Slyke and Bosworth[1] of the New York Agricultural Experiment Station.

"Its operation in the determination of casein in a sample of milk requires only from twelve to fifteen minutes and the result was reasonably accurate, usually coming within 0.1 to 0.2 per cent. of the correct amount." This method requires the simplest and most inexpensive equipment. It further is eminently practical in the hands of unskilled persons after a minimum of instruction.

3. *Albumin.*—Albumin when determined was found by subtracting the per cent. of casein from the per cent. of total proteins.

STUDY OF PERCENTAGES OF CASEIN IN LABORATORY MILK FORMULAS

In Table 1 will be found the results obtained from the examination of twenty mixtures obtained from a food laboratory. These were made from

* From the Massachusetts Babies Hospital, 106 Chestnut Avenue, Jamaica Plain, Mass.

1. Van Slyke and Bosworth: New York Med. Jour., Sept. 18, 1909.

32 per cent. cream, fat-free milk, whey, etc., from a reliable source. In each case the prescribed formulas are given, while in the last column the amounts of variations from these formulas are seen. It will be noticed that in every case the total protein found was less than that called for. No determinations of fats or sugars were made. If as much error

TABLE 1.—PERCENTAGES OF CASEIN, ETC., IN LABORATORY MILK FORMULAS

Sample	Formulae Prescribed			Found		Error
	Fat	Sugar	Protein	Casein	Protein Total	
1	4.0	7.0	1.50	1.1	1.2	(—) 0.3
2	4.0	6.0	1.60	1.3	1.4	(—) 0.2
3	4.0	7.0	2.50	1.5	2.1	(—) 0.4
4	4.0	7.0	2.00	1.4	1.8	(—) 0.2
5	2.5	7.0	.50-1.20	1.4	1.4	(—) 0.3
6	2.25	5.0	.90-0.25	0.3	0.9	(—) 0.2
7	1.70	7.0	0.89	0.7	0.7	(—) 0.1
8	2.75	6.0	1.25	0.9	0.8	(—) 0.4
9	4.0	7.0	1.50	1.0	1.0	(—) 0.5
10	3.9	6.5	2.10	1.3	1.6	(—) 0.5
11	4.0	7.0	2.00	1.4	1.6	(—) 0.4
12	3.75	6.75	1.50	1.2	1.2	(—) 0.3
13	3.60	6.50	.90-0.50	0.7	1.0	(—) 0.4
14	4.0	7.0	2.25	1.4	1.9	(—) 0.3
15	4.0	7.0	2.50	1.5	2.2	(—) 0.3
16	3.75	6.75	.90-1.00	1.2	1.7	(—) 0.2
17	4.0	6.75	1.50	1.1	1.3	(—) 0.2
18	3.25	5.50	3.25	1.7	2.7	(—) 0.3
19	4.0	7.0	1.75	1.4	1.6	(—) 0.1
20	2.50	5.50	0.75	0.6	0.6	(—) 0.1

TABLE 2.—ANALYSIS OF PERCENTAGE CREAM AND MILK

Date	32% Cream T. P. Cas. Alb.	16% Cream T. P. Cas. Alb.	4% Milk T. P. Cas. Alb.	F. F. Milk T. P. Cas. Alb.	Whey T. P. Cas. Alb.
April 21	2.28 = 1.5 (0.78)	2.50 = 1.6 (0.90)	2.76 = 2.0 (0.76)	3.16 = 2.2 (0.96)	0.78 = 0.0 (.78)
April 22	2.10 = 1.4 (0.70)	2.58 = 1.5 (1.0)	2.88 = 2.1 (0.78)	3.08 = 2.1 (0.98)	0.87 = 0.0 (.87)
April 23	2.17 = 1.5 (0.67)	2.70 = 1.7 (1.0)	2.97 = 2.1 (0.87)	3.19 = 2.2 (0.99)	0.87 = 0.0 (.87)

occurred with them as was found with the protein, many of the formulas would have been very deficient in caloric value. These errors we at first put down to irregularities in the milk and cream used in making the mixtures. On examination of these products, however, we found that they

were fairly uniform in composition, as is shown by the figures in Table 2. The greatest variations are found with the creams, but the actual error caused by these variations would be very small, as the creams are always diluted with the other ingredients in the mixture.

STUDY OF PERCENTAGES OF CASEIN IN HOME MODIFIED FORMULAS

Table 3, in contrast with Table 1, gives the results of examination of fifteen home modifications. These were made from 10 per cent. cream and fat-free milk which were furnished by a reliable dairyman. It will be noticed that only six of the fifteen mixtures contained less protein than

TABLE 3.—ANALYSIS OF HOME MODIFICATIONS

Sample	Formulae Prescribed			Found		Error
	Fat	Sugar	Protein	Casein	Total Protein	
1	2.0	6.0	1.00	0.85	1.05	( ) 0.0
2	2.0	4.0	1.50	1.4	1.85	(+) 0.3
3	2.5	6.5	2.75	2.0	2.8	(+) 0.1
4	1.25	6.5	1.25	1.0	1.37	(+) 0.1
5	2.0	6.5	1.2	0.85	1.16	(—) 0.1
6	1.75	7.0	1.5	1.2	1.5	(—) 0.0
7	2.0	6.5	1.5	1.3	1.7	(+) 0.2
8	3.25	7.0	1.75	1.1	1.6	(—) 0.1
9	2.0	6.5	1.6	1.0	1.4	(—) 0.2
10	1.25	6.5	1.2	0.8	1.1	(—) 0.1
11	2.0	6.5	1.6	1.4	1.8	(+) 0.2
12	2.25	6.5	1.6	1.0	1.4	(—) 0.2
13	3.25	7.0	1.7	1.2	1.6	(—) 0.1
14	2.0	7.0	1.5	1.1	1.5	( ) 0.0
15	2.0	3.0	2.0	1.7	2.2	(+) 0.2

the formulas called for, while the average error is much less than in the case of the mixture prepared in the food laboratory. We can give only one feasible explanation for the variations and deficient proteins found among the laboratory formulas, i. e., that there is a lack of careful technic on the part of those concerned in making the mixtures correspond more closely to the prescribed formulas.

POSSIBLE METHODS OF OVERCOMING THIS DEFICIENCY OF PROTEIN

There are three methods of making up formulas which will give a more exact casein content: (a) Secure cream and skimmed-milk from a reliable dealer and have him furnish proper analysis of the same. From

the analysis a mixture of any desired composition can be made with a few simple calculations. This method is recommended for home use under the direction of a physician. (b) Recommended for hospitals and institutions: Secure cream and fat-free milk. Determine the percentage of fat in the cream by the Babcock test. Determine the percentages of casein in the cream and fat-free milk by the volumetric method of Van Slyke and Bosworth.

The percentage of casein multiplied by 1.4 would give the percentage of total protein (or a figure which is close enough to it for all practical purposes). By the use of simple calculations, mixtures can be made which will vary from the formula by about 0.1 of protein. (c) This method is in the experimental stage and is not recommended for general

TABLE 4.—ANALYSIS OF FORMULAS IN AUTHOR'S EXPERIMENTS

Experiment	Date	Formula			Protein in Food by Analysis	Volume Taken	Nitrogen			
		Fat	Sugar	Prot.			Ingested gm.	Excreted gm.		Retained gm.
	April							Urine	Feces	
1	12	2	4	2	1.93	1134	6.9	4.90	.54	1.46
	13	2	4	2	1.93	1134				
2	16	2	4	2	1.90	1134	6.8	4.21	.39	2.20
	17	2	4	2	1.90	1134				

use at present. The desired mixture is made by using the necessary amount of cream, whey, etc., and dry powdered casein or paracasein. The percentages of fat and protein in the cream are determined and the whey is assumed to contain 0.9 per cent. protein. (N. B. It is quite important that some whey be used, as it furnishes the inorganic constituents demanded by the growing baby. The proper amount of whey to be used has not been accurately worked out as yet.) The amount of protein necessary to complete the formula is secured by adding in the form of dry powder, casein or paracasein.[2]

EXPERIMENTS WITH DRIED POWDERED PARACASEIN

One of the preliminary experiments which was carried out is seen in the following. It was undertaken to determine the digestibility of formulas made with dry powdered casein.

2. Bowditch: Boston Med. and Surg. Jour., May 15, 1913, p. 722.

The patient, H. A., was admitted to the hospital Jan. 15, 1913, for observation and feeding. The child was apparently normal, fair physical condition, development and digestion. April 12 the experiment was started. Up to this time the child had been gaining well. His movements were one to two a day, normal, giving no signs of fat, carbohydrate or protein indigestion. His temperature was normal and disposition happy. On April 12 he was placed on the metabolism bed. The food given from April 12 to 16 was made from ten per cent. cream, fat-free milk, lactose and water and had the composition indicated in Table 4 (Experiment 1). Urine and feces were collected for a forty-eight hour period, the feces being marked off by carmin red. The figures obtained are also given as Experiment 1, Table 4. The child took the food well, had no temperature, gained in body weight and remained normal in every respect. On April 16 the food was changed. The percentage composition remained the same, but the materials used were different; cream, whey, lactose, lime-water and dry powdered paracasein. The food was well taken, the child's well being and general condition continued normal, no rise in temperature developed, he gained in weight and his movements were perfectly smooth and digested, but more formed. The urine and feces were collected for a period of forty-eight hours as before and the figures obtained are given as Experiment 2, Table 4.

From the foregoing we can safely say that laboratory formulas are frequently deficient in protein; that home modified mixtures compare far more favorably on this point. That it does not seem to be the fault of the constituents which go to make these mixtures, but rather the care of those who put up such formulas.

We feel that we have proved that formulas with exact percentages of protein can be obtained by determining the percentage of casein in the creams and milks used, and further, that powdered dry casein and paracasein can be used in making up shortage of protein in place of fat-free or skim-milk. We will also show in a later publication that this powdered dry casein or paracasein is very easily digested, and is capable of furnishing all the protein requirements of the growing baby.

This procedure of accurate determination of protein may or may not be of service. It remains to be seen how far it can be used. It is certainly not necessary to go into such details in general, but special cases may bear more fruit when we consider the possible errors and the resultant underfeeding of protein as we have illustrated above. This is the beginning of a series of experiments to be continued along similar lines.

We wish to express our thanks to Dr. Helen Dudley of Brooklyn, New York, for her interest and time.

THE INFLUENCE OF VARIATIONS OF DIET ON GASTRIC MOTILITY IN INFANTS

MAYNARD LADD, M.D.
BOSTON

Radiographs of an infant's stomach, taken at regular intervals after a bismuth meal, offer a new and interesting method of studying gastric motility. By means of serial views, we may obtain exact data not only of the time required for complete emptying of the stomach, but of the rate at which the food is expelled. By varying the composition of the food, we may form an opinion of the effects of the different milk elements on gastric motility. Moreover, if the same conditions of the experiment are maintained, we may determine differences in the effects of certain formulas in several babies of approximately the same age.

In a paper which I read in February before the Tristate Medical Association at Norfolk, Va., I gave the result of my observations of gastric motility based on a study of fourteen infants, making a series of twenty-four experiments, in which about 125 radiographs were taken. Since then I have increased the number of observations by about 100; so that the ideas embodied in this paper are based on approximately 225 radiographs of infants' stomachs, showing various stages of digestion. The object of these earlier studies was to determine the appearances of infants' stomachs during digestion so far as they could be demonstrated by the Roentgen ray, as we have as yet very little data by which to judge of normal and abnormal appearances by this method of investigation. There are so many factors on which gastric digestion depends that it is a slow and laborious undertaking to gather sufficient data on which to base conclusions. The age of the child, the quantity of food administered, the composition of the food, as shown by variations in the percentages of its elements, by alterations in its reaction, by addition of such ingredients as whey, barley water, etc., by the use of precipitated caseins instead of the natural proteins of milk—may all be factors influencing gastric motility. Then, again, there are the individual peculiarities of the child. It is evident from the work I have already done that two infants of the same age, taking the same formula and quantity, may show very different gastric conditions as regards motility.

One of the first points observed in these radiographs is the curious lack of peristalsis to be seen in a normal infant's stomach, as compared with that of adults. The stomach appears to squeeze out its food by contracting as a whole on its contents, seldom showing the marked indentations so characteristic of the peristaltic waves in the adult. In the normal case, some of the food appears in the small intestines as soon after the feeding as the plate can be taken. The emptying process goes on rapidly at first, the major part of the contents being expelled in from one and one-half to two and one-half hours, both in breast-fed and bottle-fed babies. After two hours the emptying process is relatively slow in the majority of cases, often requiring from four and one-half to five and one-half hours, or even longer, before all traces of bismuth have disappeared. In one case, a normal baby, there was a considerable residue of food after seven and one-half hours.

This condition of relative inactivity of the stomach as regards motility after the first two hours appears to be due in part to the character of the food, in part to the lack of sufficient distention of the stomach, which seems to be a factor in stimulating peristalsis. If an infant is given a bismuth feeding and then at the end of three hours another feeding without bismuth is administered, the new feeding does not mix intimately with the bismuth residue of the earlier feeding, but appears to stimulate the contraction of the stomach as a whole, and the expulsion of the bismuth residue is accelerated, pushed out, as it were, by the new feeding. This expulsion is not immediate by any means, but is more rapid than if the stomach is allowed to empty itself without the stimulus to peristalsis which the new feeding imparts. On the other hand, one may show that if the new feeding is given so soon that the stomach has not had time to get rid of a large part of the first bismuth feeding, the overdistention which results produces a condition of inactivity or stasis and the emptying time of the stomach is prolonged.

This interesting action of the stomach is, I think, an important factor in explaining why the results of feeding infants at short intervals, such as two and and two and one-half hours, may in some babies be successful, in others not. The normal emptying time, even in breast-fed infants taking the same quantity of food, varies within wide limits. In the case of Randolph it was two and one-half hours; in Laffey, five and three-fourths hours; in Koar, five and one-fourth hours. An interval of two hours in the first case would find the stomach nearly empty of its

contents, and the new feeding, by exciting peristalsis, would hasten the exit of the residue that remained. In the other two babies a two-hour interval would find a large residue remaining from the previous feeding, so that the addition of a new feeding might readily overdistend the stomach and produce a condition of stasis, from which vomiting might easily result. I have not found, as yet, a child whose stomach was completely emptied in two hours. It is an exceptional case even when it is emptied before three and one-half hours. If the peristaltic action is not stimulated by a new feeding, the emptying time is much more likely to range from four and one-half to five and one-half hours (or even longer), but as we shall see, the character of the food is an important factor in determining the time required.

The statement that the stomachs of breast-fed infants are emptied in two hours and of bottle-fed infants in three hours, cannot in the light of these bismuth experiments be considered as even approximately exact. On the other hand, I think the advocates of four-hour feedings are mistaken in assuming that such an interval allows the stomach one hour of complete rest between feedings. In many cases there is nearly as much residue after four as after three hours. This is particularly true if the formula contains high percentages of casein. The question of three- or four-hour intervals between feedings cannot be settled by *a priori* reasoning, but may well be left to one's experience with the individual child.

The objection may be raised that the bismuth alone may account for the apparent residue in these cases. I think this is disproved by careful observation. In the case of Randolph, a formula was given on two successive days (2.1 per cent. fat, 6.6 per cent. lactose, 0.90 whey proteins, 0.60 casein). On the second day the dose of bismuth was doubled without influencing the emptying time of the stomach, which for this particular formula was two and one-half hours. Again, this same baby was given the same amount of bismuth in a formula calling for 0.0 per cent. fat—6.6 per cent. lactose—3.5 per cent. protein, and there was a considerable residue seven hours later. This specific instance, and many others, have convinced me that in a normal stomach the bismuth does not of itself retard peristalsis or in any way interfere with gastric motility. This statement is true of the subcarbonate of bismuth in doses up to two rounded teaspoonfuls. I have had no experience with larger amounts than this in infants. These large doses do not constipate

the baby or cause indigestion. In my last series eighteen rounded teaspoonfuls were given in the course of thirteen days without ill effect.

From my recent work on the effect of variations of fats and proteids on gastric motility, the results of which, as far as I have been able to carry it, I shall give, two conclusions may be stated with confidence.

First. There are individual variations in gastric motility independent of the composition of the food. Two infants, for example, showed an emptying-time, in one (Randolph) of two and one-half hours, in another (Koar) of five and one-half hours. The same infants, on a modified milk (2 per cent. fat, 6.6 per cent. lactose, 0.90 whey protein, 0.60 casein), showed an emptying-time of two and one-half hours and three and three-fourths hours, respectively.

Second. In the same baby variations in the composition of the food have a decided effect on gastric motility. For example, Randolph, whose stomach was emptied in two and one-half hours when the food was 2 per cent. fat, 6.6 per cent. lactose, 0.9 whey protein, 0.60 casein, required six and one-half hours to dispose of the gastric contents when the proteins were changed to 3.5 per cent., the formula otherwise remaining the same.

As there are these individual variations, and as the composition of the food enters into the results, it is necessary, if one is to judge of the effect of diet on motility, to carry out a series of observations on one baby, repeating the experiments in other babies of about the same age and under approximately the same conditions. This I have done in the three cases—Randolph, Pearlmutter and Koar. The first and last were taking breast milk; the second was bottle-fed. All three were within one month of the same age (7 to 8 months). Randolph and Pearlmutter took 5 ounces in the test-meal; Koar, who was 3 or 4 pounds heavier, took 6 ounces. The amount of bismuth subcarbonate was the same in each test, two rounded teaspoonfuls. In each case the bismuth was given in 2 ounces of milk by a stomach tube and the remainder of the feeding was given from the bottle. The first plate was always taken immediately after the end of the feeding, the remaining plates generally at one-hour intervals. The time was computed from the beginning of the feeding. When there was reason to think that the last plate overran slightly the period of complete emptying, the emptying-time is expressed as so many hours *minus*. When the last plate showed practically an empty condition, slight traces only of bismuth remaining, the emptying-

time is expressed as so many hours *plus*. The infants were normal and well developed and free from digestive troubles.

The results of these observations may best be shown in tabular form. For various good reasons, I could not carry out the full number of food tests in each case.

If these results are carefully studied, certain very striking facts are brought out. Whether they will hold in a larger series of cases we must wait and see. First of all, in the case of the proteins, it is quite evident that the amount of casein, when it is in a coagulable form, is the most important factor in delaying the emptying-time of the stomach. (I shall refer to the formulas according to their numbers.)

TABLE SHOWING THE EMPTYING-TIME (IN HOURS) OF THE STOMACH IN INFANTS ACCORDING TO VARIATIONS IN THE FOOD FORMULAS

No.	Formula	Fat	Lactose	Protein		Laffey 7 mos. 5 ozs.	Randolph 7 mos. 5 ozs.	Pearl-mutter 7 mos. 5 ozs.	Koar 8 mos. 6 ozs.
1	Breast milk ...	*	.....	.....	.....	5¾	.....	.....	5¼
2	Breast milk ...	2.0	6.6	1.50	.....	...	2½	.....	.....
3	Modified milk..	2.0	6.6	90/60	.....	...	2½+	4½	3¾
4	Modified milk..	4.0	6.6	90/60	.....	...	4½	4½—	.....
5	Modified milk..	0.0	6.6	90/60	.....	...	4½+	3½	3½
6	Modified milk..	0.0	6.6	3.50	.....	...	7½+	4½	6+
7	Modified milk..	2.0	6.6	3.50	.....	...	6½+	4½	5¼+
8	Modified milk..	0.0	1.5	3.50	Lactate of casein....	...	.....	3½	.....
9	Modified milk..	0.0	6.6	3.50	Lactate of casein....	...	.....	2¾	3¼+
10	Modified milk..	2.0	6.6	3.50	Lactate of casein....	...	.....	.....	3½+
11	Modified milk..	0.0	6.6	3.50	0.75 starch	...	.....	3½	.....
12	Modified milk..	2.5	6.6	1.50	0.75 starch	...	.....	2½	5¼+
13	Modified milk..	0.0	6.6	3.50	(Precipitated casein) Bowditch				

* Composition unknown.

In the case of Randolph, breast milk of known composition was emptied in two and one-half hours. A modified milk of the same composition, using a whey mixture with the amount of casein as estimated in the breast milk, was emptied in two and one-half hours plus. In Nos. 6 and 7, with a total protein of 3.5 per cent., the emptying-time jumped to seven and one-half and six and one-half hours plus. The effect of fat is also shown in this series. Note that in No. 5, with no fat, the emptying-time was prolonged to four and one-half hours plus.

In No. 4, with 4 per cent. fat, it was four and one-half hours, but in No. 3 it would seem as if a moderate amount of fat, i. e., 2 per cent., favored the expulsion, as the emptying-time was only two and one-half hours plus. In Nos. 6 and 7 the same is true, i. e., with 2 per cent. fat the emptying-time was one hour shorter.

In the second case (Pearlmutter) no breast milk was available. The child had always been fed on strong modified milk with total proteins. This child seemed to have more casein toleration. As seen in Nos. 3, 4, 6 and 7, the emptying-time was uniformly four and one-half hours, irrespective of the percentage of casein, or of the percentage of fat. An exception is seen in No. 5, when in the whey mixture without fat the emptying-time was three and one-half hours, but the more rapid emptying-time is undoubtedly due to the low percentage of casein.

In Nos. 8, 9, 11 and 12, I tried the effect of giving the casein in a modified form in the first two formulas, using the precipitated casein, as it occurs in lactic-acid milk; and in the last two using barley starch to make the curd in the stomach small and flocculent. In Nos. 8 and 9 the emptying-time was from one to one and one-half hours shorter. In the case of the barley mixture, the results were even more striking. I do not, however, lay too much importance on the apparent shortening of the time here, because the plates were not so definite that I could assert with positiveness that the bismuth was all in the intestines and not in the stomach. Unsatisfactory radiographs will now and then inevitably result, despite the best efforts of a conscientious roentgenologist.

In the third case, Koar, who previous to these experiments had always had breast milk, one sees, as in the case of Randolph, a greater susceptibility to the action of casein. The emptying-time on breast milk—of unknown composition—was, as seen in No. 1, five and one-fourth hours. On Nos. 3 and 5, with a whey mixture of low casein percentage, the emptying-time was three and three-fourths and three and one-half hours, or from one and one-half to one and three-fourths hours less than when given breast milk. In No. 6, when the proteins were raised to 3.5 per cent., the emptying-time rose to six hours plus—nearly one hour more than on breast milk, and nearly double the time required when the casein was 0.60 per cent.

Again, in this case, as in Randolph, we see the marked reduction in the emptying-time (Nos. 9 and 10). When the protein was given in the form of precipitated casein (lactic-acid milk), being three and one-

fourth and three and one-half hours only as compared with six hours when no effort was made to alter the curd. In No. 12, with barley starch, the emptying-time was the same as on breast milk; that is, five and one-fourth hours.

One does not draw definite conclusions from such a series of cases, but the suggestion is strong that the casein of cow's milk, when given in high percentages, has a decided action in prolonging the emptying-time of the stomach. If this casein is precipitated outside the body, the emptying-time is greatly accelerated. The presence of fat has no retarding action, and in some cases seems to favor the exit of the stomach contents. There is some reason to believe that barley starch renders the food more easy of exit.

In concluding, I wish to express my thanks to Drs. Percy and Wyman, house physicians at the Children's Hospital, who have by their interest and cooperation relieved me of much routine work. And particularly, I wish to thank Mr. Mulvaney, the assistant roentgenologist, to whose credit entirely the radiographs are due.

270 Clarendon Street.

DISCUSSION OF PAPERS OF DR. HENRY I. BOWDITCH AND DR. MAYNARD LADD

DR. GRAHAM: I have done some work analogous to Dr. Ladd's, but I am not satisfied with the Roentgen-ray photographs. It seems to me that one must be very careful about the conclusions one draws, for serial radiographs are very apt to show the bismuth meal remaining in the stomach a much longer time than does the ordinary meal. I was much interested in some of his bismuth radiographs showing that the meal left the stomach entirely at the end of 2½ hours. In the large majority of children to which I have subjected this test, I have found the tendency has been for the bismuth to remain in the stomach a considerably longer time than 2½ hours, and I doubt if it is possible for us to draw any conclusion as to the definite time which should elapse when working on these subjects. If an infant is given a second bismuth feeding three hours after the first it rushes the previous meal out of the stomach so that the tendency would be for a single meal to remain a considerably longer time.

DR. PISEK: I would like to ask Dr. Ladd in what position the children were when the pictures were taken? Whether held up to the plate, or prone—face downward?

DR. CHURCHILL: Dr. Ladd has given us the quality of food but he has not given us the quantity. I should like to ask Dr. Ladd how many tests of the breast milk were made in the cases in which the breast milk was taken? What is the quantity of the test meal, and how long does it remain in the cases in which breast milk is taken?

DR. BOWDITCH: To answer Dr. Griffith, I think the average amount of casein in creams and milks, as we tested them, was quite consistent with our general belief—about 2.3 or 3.4 per cent., the albumen or whey being 0.9.

The reason the heavy creams should have a greater variation has possibly two explanations: One is, we did not get the heaviest centrifugalized cream. If you should get 54 per cent. centrifugalized cream you would get little or no albumen, which under these conditions would be more exact. The second explanation is that in the process of centrifugalization your creams, unless the heaviest, have irregular amounts of proteids. In this way the proteids are thrown backward in the process and squeeze the fats out irregularly, making fats and proteids of irregular percentage. We thought it would be interesting to show the different samples as we made them and I am glad to show you these specimens. It happened that in making formulas for the babies in the laboratory, the dietitian was found throwing away material which occurred to me could be utilized. I had her save the curds and these were dried and ground. From an economical point of view, if one could save the curds, dry and grind them, a laboratory like the Walker-Gordon could save something like $600 to $1,000 a year. We were able to get two or three pounds of dry casein from 48 to 50 quarts of milk per day. I have found, as far as I have been able to go, that children with gastric symptoms of vomiting, regurgitation, etc., have done very well on dry casein. These symptoms have cleared up very rapidly. The food was taken just as easily as though the casein had been dissolved in water. I was somewhat cautious in trying this at first, but certainly I have found that the dry casein is safe and may be even better than moist casein in certain cases.

DR. LADD: In reply to one of the questions I will state that the radiographs of the children were taken lying on their stomachs and in the intervals between exposures the babies were lying on their backs in their natural position. In regard to Dr. Churchill's question, the quantity of food that was given was 5 ounces at a feeding, with the exception that the last child, who weighing several pounds more than the others, received 6 ounces. It was not the child that had the largest amount of food at the feeding that retained the food longest in the stomach.

A CASE OF ERYTHROMELALGIA

S. S. ADAMS, M.D.
WASHINGTON, D. C.

The patient, a little girl, was born Aug. 2, 1910, and was perfectly well until February, 1913. At that time she developed a painful rash that existed about a week. It covered the entire body and was very red. Two physicians who were consulted called it "small hives." From that time the child had very little appetite and was more or less listless. About March 1 the lassitude increased, she ate very little and her sleep was disturbed at night. A few days later she complained that she had pain in her head and she began to sleep with her hands clasped under her head.

March 5 Dr. D. was called and prescribed calomel and bromids without any satisfactory result. The child became gradually worse, and then this physician acknowledged that the disease baffled him and advised a consultation. About this time the pain in the head ceased, but the child required continual massage of the feet. Moreover, the hands and feet were slightly swollen as well as red. March 17 Dr. F. examined the child and pronounced the organs sound. He found only anemia and a tonic was prescribed. March 26 Dr. K. was consulted and suspected tuberculous meningitis, but by this time Dr. D. was confident that the disease was pellagra, of which he had only read. During all this time the child's temperature was never above normal and had a tendency to be subnormal. There was no complaint by the child about her hands, although she cried out when they were touched and kept them elevated and apart from each other. She complained continually of pain in her feet and asked to have them rubbed or scratched. April 1 she was brought to Washington and was first seen by me. At the present time, April 15, the redness is disappearing from the hands and feet, and there is a scaling of the hands, with the formation of new skin underneath. The appetite is improving and the child is apparently gaining weight.

When seen by me there had been so much pain in the feet that the child had to be carried about all night long. The hands were red as far as the wrists and she cried out when they were touched, but the moment they were exposed to the cold air the pain ceased. The feet were similarly

affected and looked as if gangrenous spots might appear, but they also were relieved by exposure to the cold. My diagnosis was either angioneurotic edema or erythromelalgia, but I thought the latter better fitted the case. I placed the child on a diet, gave her a mixture containing hydrochloric acid and sent her to Virginia, where it was treated as pellagra. I now have a case in the Georgetown University Hospital, but the symptoms are not at all similar. I have asked the parents to bring her here to-day, and as she is here now I would like to present the case to the society. (Exhibiting the child.) You see the petechial spots still remain, but the child has improved.

The subsequent history of this case is well given in a letter from the child's father as follows:

EDINBURG, VA., June 18, 1913.

Dear Dr. Adams: I was away from home when your letter arrived, which accounts, in fact, for my tardiness in replying.

Answering your inquiry: Her improvement since you saw her last has been steady. She seems to have returned to her former condition of activity and liveliness. Her appetite is good though somewhat irregular—also her habits are satisfactory. Her weight increases very slowly. About February 1 she weighed near 30 pounds—to-day she weighs but 33 pounds. She displays an unwonted nervous tendency, especially when butterflies and bumble bees fly about her. Her skin is smooth and fair as aforetime and she shows no sign of her late trouble. The first two weeks of this month she spent in the country with her mother and while there drank milk as she will not at home, though the cow that supplies her here is first class. For two weeks now she has taken no medicine and does not seem to me to need any. On August 2 she will be 3 years old.

Yours gratefully. H. E. C.

This case may yet develop into one typical of pellagra, but until it does I think I am justified in adhering to my original diagnosis.

DISCUSSION

DR. LOVE (Guest): (After examining the child.) I can add little to what Dr. Adams has said on the subject. I should say, however, that the dermatitis is almost typical of pellagra both as to appearance and distribution, and if I had seen this case in Florida I would have called it pellagra. I have a case there almost identical with this case. The nervousness referred to by the father is characteristic of pellagra, but of course in a child it is very difficult to judge of the mental depression. I think it is a case that may be diagnosed as a mild case of pellagra.

DR. WESTON (Guest): I do not think I can add anything to what has been said except that I believe the diagnosis of pellagra is correct, and I will add that if the father of the child does not make a change in the child's diet, the same condition will appear next spring about the same time as it appeared this year. In the cases of pellagra that I have seen in young children diarrhea is not at

all constant, for constipation may also exist. We know that if a person is fed almost constantly on corn flour it will cause pellagra.

DR. DE BUYS (Guest): I think that diarrhea is one of the diagnostic points of pellagra, but it seems that diarrhea is absent in this case; also, the discoloration of the skin we frequently find is absent. However, the case looks more like a mild case of pellagra than anything else. If it is, the child has probably passed the crisis of the attack.

DR. ACKER: Do the symptoms recur?

DR. DE BUYS: Yes. There is a tendency to the return of the symptoms as the warm weather begins in the spring.

DR. ACKER: When does the parchment condition occur?

DR. DE BUYS: Usually during the height of the disease.

DR. ADAMS: Assuming that this attack has not passed over, it has passed its crisis, has it not?

DR. DE BUYS: Yes. I might say that we have at this time some one in Washington attending the Congress, Dr. C. C. Bass, who has probably done more in the study of this disease than any other person I know of, and if it is the desire of this Association I will make it a point to see him and have him at one of your future meetings to see this case.

DR. ADAMS: I admitted to the father that I had never seen a case of pellagra in a child but that I had seen the disease in an adult. I thought you gentlemen from the South were better able to teach us in regard to this disease than anything else. The erythromelalgia was complete when I first saw the child and I diagnosticated it as that because of the intense redness of the skin and pain and the crying of the child and restlessness at night, and all the other symptoms of the pain that the child had of the feet and hands, and the relief by the cold air. These points guided me in making this diagnosis.

I am informed that the child has not been fed on any corn flour, and she is undoubtedly better than when she came under my attention. If this is a case of pellagra, of which I am not convinced, I may be excused for the error in diagnosis because it has been my misfortune to have seen but one case of the disease.

ACUTE INFECTIOUS JAUNDICE IN CHILDREN

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In this paper I desire to emphasize the fact that there is a form of jaundice which occurs in children which has all the characteristics of an acute infectious disease. Many of our text-books still speak of this disease as a gastroduodenitis due primarily to indiscretions in diet. The infectious material, as yet unknown, seems to have an affinity for the bile passages in the same sense that the typhoid bacillus has for the follicular structures in the intestines.

The following report is based on ninety-eight cases seen during the last six years, chiefly at the Vanderbilt Clinic and at the Lebanon Hospital Dispensary. Twenty-five were seen during October, November and December of 1912 and January, 1913. These were studied more carefully, and it is on them that the following data are chiefly based.

Age Incidence (Chart 1).—In the series of ninety-eight cases there was no patient under 1 year of age. The disease is exceedingly rare in young infants. Between 1 and 2 years the disease is uncommon—only two patients in ninety-eight. It is most common between the ages of 3 and 6. After that the number gradually diminishes.

Seasonal Incidence (Chart 2).—It will be immediately noted that the disease is especially prevalent during October, November and December, over one-half of the cases occurring during these three months. This fact alone would be a strong argument in favor of its infectious nature. Indiscretions in diet are certainly not more common in October and November. In Chart 2 I have added the curve of seasonal incidence drawn from the figures given by Flesch in a series of 188 cases recorded as occurring during a period of ten years at the Stephanie Hospital in Budapest. It will be seen that the curve corresponds very closely to my own. Several authors have noted that the disease is more prevalent when the autumn and winter are mild. This would hold true for our epidemic of last year in New York City.

In none of the last series of twenty-five cases was I able to ascertain that there had been any gross indiscretion in diet just previous to the attack, and in only three of the patients was there a history of previous

attacks of indigestion which might indicate a predisposition. If the disease was dependent on digestive disturbances we should expect it to be more common during the summer months, a time when, as the chart shows, the fewest cases occur. The disease is rare in infancy, when gastro-intestinal disturbances are most frequent. Even when the duodenum is markedly affected, jaundice does not result. In several of my patients there was no digestive disturbance at any time during the attack, and in ten of the last twenty-five, after the disturbance at the onset, the appetite was good and there was apparently no change whatever in the digestive functions. The vomiting, which is frequently present at the beginning, is probably toxic.

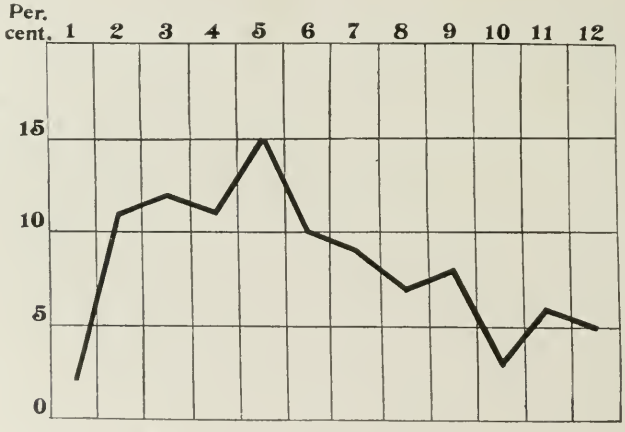

Chart 1.—Age incidence of acute infectious jaundice.

Bacteriology.—The specific micro-organism, if there is one, which causes this disease, has not yet been isolated. Jaeger, in a case of Weil's disease, found a *Bacillus proteus fluorescens*. Banti cultivated from the blood obtained by puncture of the spleen a capsulated bacillus which he called *Bacillus icterogenes*. Jaeger considered this identical with the one he had described. Possibly the examination of blood cultures and duodenal contents obtained by aspiration, by means of the duodenal catheter, may throw more light on the etiology.

Many authors have considered it most likely that the infection takes place through the digestive tract, on account of the initial gastric disturbance and the connection between the duodenum and common bile duct. However, this is not conclusive. From the fact that climatic

conditions seem to play such an important part in the seasonal incidence of this disease, it is not unlikely that the infection takes place through the nasopharynx.

Onset.—The most frequent symptoms at the onset were headache, lassitude and anorexia, with vomiting and some rise of temperature. In only three of the last twenty-five cases was it distinctly stated that the patient had no fever. In thirteen there was vomiting, in eight no vomiting, and in the remaining four vomiting occurred once after the taking of a dose of castor oil.

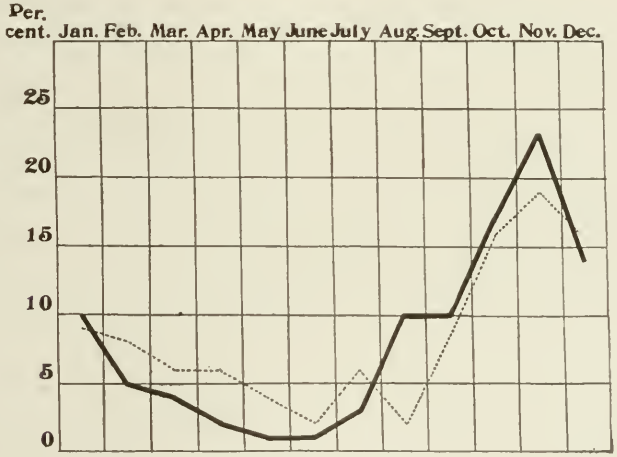

Chart 2.—Seasonal incidence of acute infectious jaundice.

Symptoms. Fever.—At the time of observation the temperature was normal in six patients, from 99 to 100 F. in eight, from 100 to 101 F. in eight and over 101 F. in three. As three of the six patients with a normal temperature were seen four or more days after the onset, it is not unlikely that they may have had some rise of temperature previously.

Pulse.—In none of the patients was the pulse slow. This peculiarity of the pulse in the jaundice of children has been pointed out by a number of observers. In those patients who had a distinct rise of temperature the pulse was correspondingly increased. This may be due to the infectious character of this form of jaundice, as against other forms of obstructive jaundice more common in the adult.

Pain.—Pain in the abdomen or epigastrium was noted in ten of the twenty-five patients; pain in the legs in three.

Urine.—The urine became darker on the first day of the disease in two patients, on the second day in two, on the third in nine, on the fourth in five, on the fifth in three and on the sixth day in two patients. In the remaining two the day was not noted. The color of the urine returned to the normal in one week in eight patients, in two weeks in eight and in three weeks in eight patients. In one the time was not noted. In three cases the examination of the urine showed traces of albumin, but no casts. The color of the urine was found to give the most convenient method of determining the improvement in the jaundice. The exact color of the stools is not easily determined, and their offensive odor makes it disagreeable for the parents to bring them. The conjunctiva remains yellow long after the improvement has begun. The method employed was as follows: Five small vials numbered 1, 2, 3, 4, 5, were used. Number 1 contained a yellow liquid of the color of the average normal urine, and in numbers 2, 3, 4, 5 there was a yellow liquid of increasing depth of color. The urine of the patient was compared with these. In this way the improvement could be readily followed and the return to the normal ascertained.

Stools.—The clay color of the stools was noted on the second day in six patients; on the third, in three; on the fourth, in three; on the fifth, in three, and on the sixth day in six patients. In four the day was not noted. As is well known, the light color of the stools is largely due to the presence of undigested fat. If fat is excluded from the diet the stools lose the characteristic clay color. The stools became normal usually at the end of two weeks. In twelve patients the *bowels* were regular; in four there was diarrhea and in eight constipation. In almost all the patients the *appetite* was poor at the onset, but after the initial disturbance had passed, the appetite was good in one-third of the patients. The *conjunctiva* was noted to be yellow on the first day in two patients; on the second, in four; on the third, in six; on the fourth, in six; on the fifth, in two, and on the sixth day in two patients. The day was not noted in the remaining three. The color returned to the normal, on an average, at the end of the third week.

Itching was present in eight. These were the patients in whom the jaundice was the most pronounced.

Liver.—The liver was palpably enlarged in twenty-one and normal in only four. It was felt one finger below the costal margin in the mammary line in four; two fingers in twelve and three fingers in five. In no

case was it distinctly painful to palpation. With the improvement in the jaundice it gradually diminished in size, but was still palpable after the jaundice had entirely disappeared.

In six patients examined three or more months after the attack, the liver and spleen were no longer palpable. In no case was it possible to palpate the gall-bladder.

Spleen.—The spleen was palpable in ten patients; not palpable in fifteen. It returned to its normal size much more rapidly than the liver.

All but one patient recovered. Only one had a serious complication, namely, an otitis and mastoiditis which required operation.

The one *fatal case* which occurred in the midst of the epidemic was in a girl of 20 months, who was admitted to the Lebanon Hospital on Nov. 30, 1912, at 10 a. m., and died four hours later. The family history was negative. There were several other healthy children. The patient had never had any acute infectious disease, the only sickness having been an attack of intestinal indigestion three months previous, which lasted about two weeks, from which the child made a good recovery. Twelve days before admission to the hospital the child had fever, vomited several times and had slightly greenish stools. One week before admission, that is on the fifth day of the disease, the mother noticed that the urine was dark in color.

I examined the child one hour before she died. The temperature was 103.2 F., the pulse 160 and the respiration 60. She was already comatose. The conjunctiva was yellow. The liver was two fingers below the costal margin in the mammary line, and the spleen one finger below in the axillary line. An examination of the blood showed white blood-cells 32,000; 95 per cent. polynuclear leukocytes. The urine obtained with catheter was acid, with a specific gravity of 1.020; dark yellow in color, with a yellow foam; albumin examination, positive; sugar, negative; white blood-cells, red blood-cells, and many hyaline, granular and epithelial casts were present. This patient presented all the symptoms of a severe infectious jaundice, a type which is usually spoken of as Weil's disease. Except for its severity it was in no way different from the milder cases. An autopsy was not obtained.

Treatment.—When the appetite is fair, as it is in many cases, it is only necessary to restrict the amount of fat in the diet. Soup, lean meat, vegetables, skimmed milk and bread may be given. It has been customary to give so-called cholagogues, but experiment has shown that most of these drugs have little or no cholagogue action. Whatever good

effect is obtained is due primarily to an increase in intestinal peristalsis. In any case the indication is not to increase the secretion of bile, but to facilitate its passage through the common bile duct into the duodenum. An increased secretion without a proper outlet would be rather a disadvantage. Bile is secreted continuously, but when the stomach is empty there is no flow of bile into the duodenum; it is stored up in the gall-bladder. When the acid chyme from the stomach passes into the duodenum it reflexly stimulates the gall-bladder to contract, the sphincter at the outlet of the common bile duct relaxes, and bile gushes into the doudenum. Some years ago a member of my family had a permanent biliary fistula following an operation on the gall-bladder. It was noted that very little bile flowed from the fistula during the day, and very much during the night. During the day the regular ingestion of food caused the gall-bladder to empty its contents into the duodenum. At night no food was taken; the bile was stored in the gall-bladder and flowed out through the fistula. The amount of bile passing out through the fistula was easily reduced by giving a small meal late at night. In a paper published in the *New York Medical Journal* for Sept. 22, 1906, I suggested that this method of giving small frequent meals might be applied in the treatment of certain biliary diseases, including infectious jaundice. Some years ago Gerhardt suggested that in some cases the distended gall-bladder could be felt and its contents expelled by pressure. The gall-bladder is so rarely palpable that this is practically impossible. However, the same result may be obtained by the giving of small, frequent meals. The character of the food is of secondary importance. I usually give five or six small meals a day, the two or three additional ones consisting of a sandwich and a glass of skimmed milk. By the use of this method I believe I have been able to shorten the duration of the disease.

250 West Eighty-Eighth Street.

DISCUSSION

DR. FORCHHEIMER: I should like to know what the blood analysis gave him, before going on. Did you find any bacteria in the blood?

DR. HERRMAN: No blood cultures were made.

DR. FORCHHEIMER: I want to say something about Gerhardt's method. It is one of the best methods for emptying the gall-bladder but it should be used rarely, for it sometimes ruptures the gall-bladder. It is a serious and dangerous procedure.

DR. HERRMAN: I do not advise the Gerhardt method, as it is a very dangerous method. I only say it is difficult to carry out.

HIRSCHSPRUNG'S DISEASE OR CONGENITAL DILATATION OF THE COLON IN A BOY OF THREE YEARS; RESECTION OF COLON; RECOVERY

HENRY T. MACHELL, M.D.
TORONTO

On June 10, 1912, I was asked to see Roy H., 3 years old, and obtained the following history: The father, mother, four sisters and one brother are alive and healthy, with no deaths. He was a full-term, breast-fed baby. His bowels did not move for three days after birth, by which time the abdomen was swollen and tense and the movement was made with difficulty. Since then, with very few exceptions, they did not move save with an enema or a purgative. At times he would go one, two, three or five weeks, and on one occasion he went six weeks without a movement, in spite of frequent enemata or purgatives. The water from the injections was not always returned, but sometimes vomiting followed. For a time glycerin injections were of benefit, yet on a few occasions it had to be repeated daily for a fortnight before an evacuation occurred. Soap and water, or turpentine and water, etc., were at times used daily, without much more success than one movement a week. During his first year cascara seemed of benefit.

The stools were frequently clay-colored and sometimes firm, but of no definite shape. They were commonly soft and pultaceous, with a little mucus at times, but no blood and very little odor.

He was usually bright and cheerful, fairly free from pain, headaches, cramps or other symptoms of toxemia. At times, however, he had occasional attacks of abdominal pain, accompanied by visible peristalsis. These attacks usually continued about five days in spite of hot applications, warm enemata, etc. During these attacks he was drowsy, vomited even water and refused all food. The vomitus was green, but not of fecal odor. He had had at least three such attacks when he seemed *in extremis*. On two of these occasions he recovered as soon as the bowels were finally moved; on the other he recovered his usual appetite and energy without an evacuation. A bowel movement was practically always accompanied by great abdominal pain and by exhaustion.

Examination showed a poorly nourished boy, who did not look more than 2 years old, of a pale gray, sallow or muddy complexion. He stood and walked in a feeble way. His abdomen was large, tympanitic over all areas, tense and shiny even in the flanks. Coils of intestine were plainly visible. An intestinal peristaltic wave was seen at times, often running from the right upper abdominal to the left inguinal region.

The abdomen measured:

Level of umbilicus, 23 inches.

Symphysis to ensiform, 14 inches.

Umbilicus to anterior superior spine, 6 inches.

Rectal examination was negative.

The diagnosis was made of congenital dilatation of the colon or Hirschsprung's disease.

As this boy had previously been in the H. S. C. under the other service and medical treatment carried out *secundem artem*, only feeding and an outdoor life were suggested till autumn, when operation would be considered.

On Oct. 21, 1912, he was admitted to my service in the Hospital for Sick Children, and after a few days transferred to the surgical side under Mr. I. H. Cameron, who advised that, as Mr. Arbuthnot Lane, the senior surgeon of Guy's Hospital, London, was coming to Canada and was to read a paper at the Academy of Medicine, Toronto, on November 5, we should wait and ask him if he would be good enough to do the operation.

On November 2 the patient was given a bismuth carbonate meal of 1 ounce and 2 ounces were injected into the bowel. Roentgen-ray pictures were taken half an hour and two hours after the meal.

On November 4 a 3-ounce bismuth meal was given at 9 a. m., and Roentgen rays taken at 9:30 a. m., 2:30 and 5 p. m.

On November 5 the patient was examined by Mr. Lane and operation decided on for the following day and iodin preparation of the abdomen ordered.

Nov. 6, 1912: For the accompanying drawing and the following description of the operation I am indebted to Dr. Hanna, Senior House Surgeon.

While Mr. Lane and his assistants, Drs. F. N. G. Starr and Beverly Milner, were scrubbing their hands, etc., and the anesthetic was being administered, two pints of normal saline were given into the skin of each axilla. Additional saline was continued at intervals throughout the operation—in all, 6 or 7 pints.

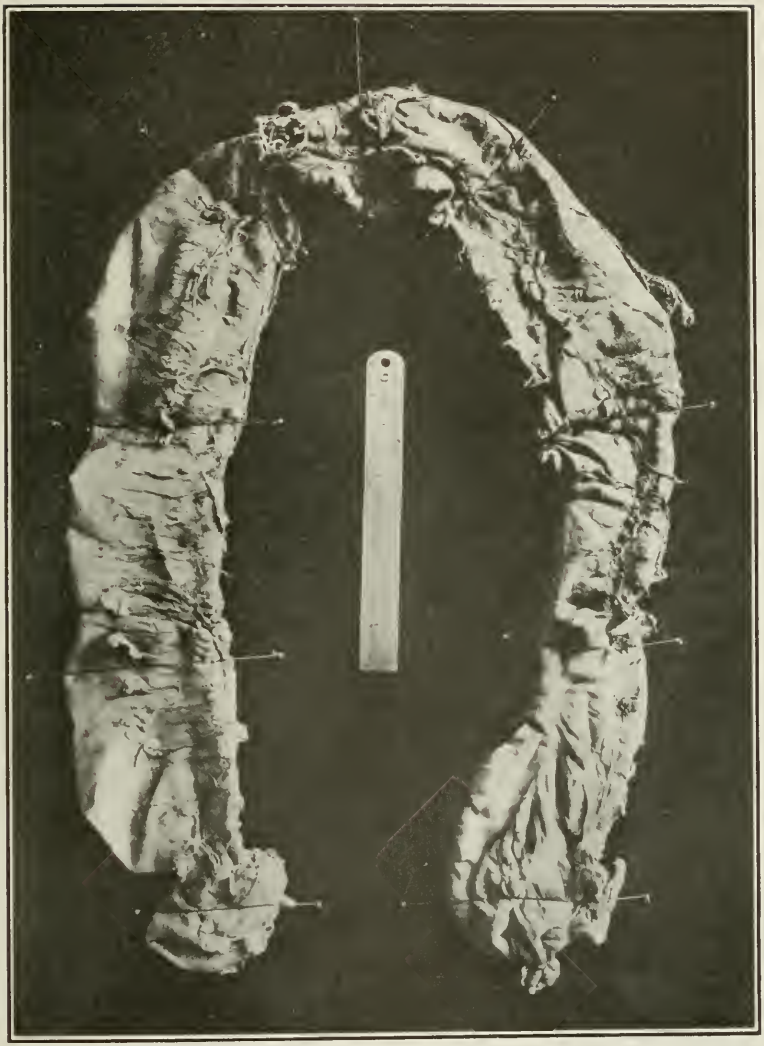

Fig. 1.—Section of intestine extending from 7 inches above the anus to 3 inches above the cecum, resected from Roy H. The appendix is seen in the lower right hand corner.

Operation.—A mesial incision was made through skin and linea alba, extending from 2 to 3 inches above the umbilicus to 2 inches above the symphysis pubis. The peritoneum was picked up and slit into its full extent of wound. The edges of the incision were now retracted. The large bowel forced its way on to the surface of the abdomen in a greatly distended condition; the intestine was covered with warmed paraffin-silk handkerchiefs. The large intestine was clamped about 7 inches above the anus; the small intestine was clamped 3 inches above the cecum; stout catgut ligatures were inserted into the mesentery at intervals and the mesentery divided after each ligature, all around. The small and large intestines were divided between the original clamps; the free end of the pelvic colon was cauterized. The large intestine was removed save a small portion of pelvic colon and rectum; the free end of the pelvic colon was sutured and a clamp was applied to the side of the colon. The free end of the ileum was brought over to the upper surface at the colon and sutured on one side, with No. 00 silk. The colon was opened and sutures were continued around the gut; a suture was now inserted, taking in all the coats of the intestine and serous coat sutured over it; a side-to-side anastomosis was thus formed.

A purse-string suture of strong gut was now passed around the free margin of the mesentery. This closed the space in the pelvis, into which the bowel might fall and become kinked or twisted. The free end of the colon was then fixed to the mesentery. A large rubber tube one-fourth to one-half-inch bore, was passed via rectum up into the small intestine about 3 inches and sutured at the anal orifice so as to anchor the tube: oz. vi of liq. paraffin were poured into the bowel through the tubing.

A small rubber tube was inserted through a stab wound in the abdominal wall to the right of the umbilicus, into the pelvis, to assist drainage.

The peritoneum was sutured, then muscles and fascia; subcuticular suture was used for the skin; lastly, a series of silkworm gut interrupted sutures was used in supporting the wound.

A normal saline compress was applied with a tight binder. The patient was returned to bed in fair condition.

No mechanical obstruction, kink, adhesion, stricture or contraction of colon or rectum was found at the time of operation to account for the distention.

Directions by Mr. Lane:

To have (1) normal saline compresses to be applied every hour to abdominal wound for twenty-four hours.

(2) Liquid paraffin, 1 ounce, to be given per oram within half an hour, in divided doses.

November 7: Directions by Mr. Lane:

To have (1) liq. paraffin, ounce i, daily by mouth.

(2) Glucose, dram i, every two hours in water, ounces ii.

(3) Liq. paraffin, ounces ii. to be given slowly through rectal tube.

(4) Normal saline every two hours.

Fig. 2.—Roy H. Taken April 29, 1913. Six months after operation.

November 8: Recovery from the anesthetic was good. His pulse improved in force and volume. The blood-pressure rose from 60 mm. Hg at the end of the operation to 80 in twelve hours. The facial expression is improved. There is less mental lassitude and apathy. The gray-drab leaden color of skin, particularly of face, is decidedly clearer, as

Mr. Lane predicted. He was allowed milk, ounce i, water, ounces iii, p.r.n., in addition to the glucose solution. Bowels acted through the tube. Abdominal drainage tube was removed to-day. Mr. Cameron advised that the present dressing be discontinued and that "Keith's dressing" be used. "Change it only if there is much oozing."

November 9: Milk was increased to 2 ounces at a feeding. Glucose mixture to be given between milk meals; no feeding at night.

November 10: Milk and broth may be given.

November 11: Condition of patient is good; wound looks healthy; bowels acting, semi-formed stools. Rectal tube removed because it was plugged and had forced its own way out, tearing out the anal stitches. May have bread and butter or biscuits.

November 16: Abdominal stitches removed last evening; wound healed and united firmly; very slight distention; bowels move daily; temperature normal. Patient now on soft diet. To have liq. paraffin one-half ounce daily.

December 8: He has been up each day for the past week. To-day the distention is about as great as before operation. The temperature has been from 100 to 103 F. for four days, even though the bowels have been moving from two to four times a day.

December 12: Though the patient has had calomel, castor oil and magnesia, and only clear broths, the distention is nearly as marked as ever and he is decidedly toxic.

December 14: The distention still continues in spite of turpentine enemata twice daily, calomel, etc. To have a lactic-acid diet of buttermilk, koumiss and lactis Bulgaricus, with an occasional soft-boiled egg.

December 18: Distention has gone down under above diet. The temperature is, however, 103 F., without apparent cause till the buccal mucous membrane was inspected and "Koplik spots" found.

December 26: The measles rash has faded and desquamation has commenced.

Jan. 8, 1913: The temperature went up to 103.4 F. this morning. Respirations, 52. There is slight generalized moisture in the chest, but no consolidation.

January 10: Temperature 105.4; P. 162, R. 60: frequent cough; marked prostration. Physical examination showed coarse and fine moist râles over back and front, both sides. The father saw the child and thought he "would like to have him die at home." He therefore removed

him from the hospital, notwithstanding the protests of the house physician. There was still some slight abdominal distention.

January 15: The patient has now well-marked bronchopneumonia and looks *in extremis*.

January 30: Has wasted markedly and is not able to hold up his head. There is no distention. He is coughing much.

February 28: Is sitting propped up in bed, râles and cough present.

March 26: The bronchopneumonia has cleared up and he is much improved, though very thin and emaciated. Is up all day. Appetite fair. No distention. Bowels move daily.

April 28: Is thriving on a mixed diet and plays out of doors with the other children.

Temperature: It will be seen by the temperature charts that it was practically subnormal from the day of entry till the day after the operation, when it rose to 101 F., but came down to normal in two days. During the next three weeks it was frequently subnormal, but more often between 99 and 100 F. On December 3 it rose to 100 F., and for five days it remained up about 102 F., and only came down to normal on the twelfth. The rise seemed due to stasis, distention and toxemia. The rise to 102 F. on the nineteenth was due to measles, then epidemic in the hospital, and from which he seemingly recovered in about a week, only to develop bronchopneumonia as late as thirteen days after his measles crisis.

Stools: The bowels moved twice in the day following operation, and practically once every day thereafter while in the hospital. At times the stools were thin and watery, at other times semi-formed. How much of the fairly free movements was due to liquid paraffin is, of course, uncertain. He had at least 1 ounce daily for six weeks, after which he had half an ounce. He took it readily. This was the remedy on which Mr. Lane placed much reliance for the easy evacuation of the bowels. We had, however, to resort to the old-fashioned calomel four weeks after the operation, when his temperature ran up, coincident with the *first* distention after the operation. Since leaving the hospital he has had no intestinal stasis or upsetting and only an occasional dose of cascara.

It has been said that diarrhea would almost certainly follow resection of the colon. It did not occur here. Neither was shock, thirst or

any discomfort complained of at any time which might be fairly attributed to the operation.

As to the mortality of the operation: Mr. Lane operated sixteen times at Guy's Hospital from June, 1909, to June, 1910, with but one death, and that was due to the bursting of an abscess from the abdominal wall into the peritoneum seven days after the operation. The majority of his operations were performed for intestinal stasis, concerning which he has written frequently and convincingly in the British journals within the last few years. How many of his operations were for Hirschsprung's disease I was not able to make out from his records. I regret that the photographs taken before the operation are, owing to rearranging of the Roentgen-ray room, stored away so carefully that they cannot, at present, be found.

The photographs taken April 29 last show the appearance of the wound and shape of the abdomen six months after the operation.

The specimen exhibited is much smaller now than when removed, owing to its having been, unfortunately, put in a formalin solution, while in a lax instead of a distended condition. My recollection of it as it rolled out on the table at the time of the operation is that it was half as large again then as it is to-day.

MEMORANDA

Ten days after reading the above paper the mother of Roy H. gave birth to a well-nourished boy, who seemed healthy in every respect.

Dr. Boyer, who looked after the mother and baby, was good enough to send me the following short history of the case: For a day or two after birth the infant seemed as well as the average one, but by the end of the third day his abdomen was noticeably distended and tympanitic. Though the bowels were moved slightly a couple of times on that day, the stools were dark, greenish, fluid and offensive. From that time on it required calomel, castor oil, magnesia or enemata to produce an evacuation, which was invariably offensive—so foul at times that the odor was positively objectionable in the hall outside the bedroom. In spite of free watery stools the distention and tympany persisted, and on the eleventh day the history states: "The abdomen is very much larger and tense, with marked tympanites, and the transverse colon stands out clearly across the abdomen as a special band of distention." There was little or no elevation of temperature, and vomiting occurred only a few times.

Though he nursed properly at times, he did not takes the breast like a hungry baby, but rather like one who had persistent colic or discomfort. From the fourth day he seemed to get thinner and paler and died fifteen days after birth.

At autopsy "the colon was found unmistakably distended from the cecum to the sigmoid, where it began to decrease in size, and ended as a normal pelvic colon and rectum"—unlike the colon of his brother Roy, which was enlarged its whole length. The distended portion measured 2½ to 3 inches in diameter. The contents of the colon were fluid, dark in color and very offensive. The wall was somewhat thicker than normal. (Sections taken.)

The baby died of intestinal toxemia.

A case of Hirschsprung's disease is seldom seen. Two successive children with this disease in the same family is, therefore, of peculiar interest. I have not been able to find such a record in the literature on this subject.

95 Bellevue Avenue.

DISCUSSION

DR. GRAHAM: I would like to ask Dr. Machell how much colon was removed? I think that the results achieved by Dr. Lane in operating for this condition in children have been wonderful, if he has had only one death in sixteen operations. I should like to ask whether these results have been attained by any other surgeon? I have had one case of this disease and it was intended to do a two-stage operation. The surgeon in this instance did a partial operation, but the child died eight or nine days after the first stage of the operation. I think it would be a good thing to decide just what the mortality of this disease is, for if others can get the results that Dr. Lane has secured, then operations would be justifiable.

DR. GRIFFITH: Dr. Machell's case is a typical instance of congenital idiopathic dilatation of the colon, and I think he is greatly to be congratulated on the result. A number of years ago I had under my care a similar case on which operation was done, but without success. Shortly afterwards (1899) I made a careful search through medical literature for cases of this disease, and reported the result before the Association of American Physicians. I could find in all but twenty-four cases which seemed to me to belong unquestionably to this category, although there were many others which by some had been placed here. Of course other cases have been reported since that time, but the condition in its strict sense is not a common one. To be true instances of Hirschsprung's disease, the dilatation must be congenital and idiopathic. To be congenital it need not be actually present at birth—although it usually is—but the inborn tendency to dilate, the idiopathic quality, must be there. There have doubtless been many cases of acquired dilatation wrongly described as instances of the idiopathic form. The dilatation must not be the result of an acquired atony from prolonged digestive disturbances, nor the result of stenosis of any sort as by compression by a tumor or the like. Even dilatation which may

follow a chronic tendency to kinking of the bowel, the result of the very long sigmoid flexure to which Dr. Jacobi called our attention years ago, is not properly included here. This form is a dilatation following stenosis: an acquired variety not an idiopathic dilatation.

As to the title often employed, "Hirschsprung's disease," there is no vital objection to it if we recognize the fact that the priority of description does not rest with this investigator. The first case on record appears to have been described by Henoch in 1861, and a number of others are on record before the published cases by Hirschsprung in 1888. Personally, I think the employment of proper names in this way is to be avoided as far as possible.

There are two characteristic symptoms, viz., *constipation* and *abdominal distentions*. They usually appear together soon after birth but either one may antedate the other. The constipation seems ordinarily to be due to a lack of power to evacuate the bowel, for the stools are seldom hard, and the insertion of a rectal tube or the giving of an injection, may bring away a very large amount of soft feces. The abdominal distention is usually relieved to some extent by evacuation of the bowel; but this is not always the case since in some patients diarrhea may replace constipation without relief.

The prognosis in the twenty-four cases in my list was very unfavorable; only two patients were known to have recovered and eighteen were known to have died. Doubtless the more prompt employment of operative measures with the improved technic has saved more in recent years; but again I feel like emphasizing the need of great caution in making a strict classification of the forms of dilatation before reaching percentage figures of recoveries. Similarly, the need of careful diagnosis is of especial importance as a guide to the necessity of any operative interference. As an illustration I may say that some years ago I was asked to see a child of 4 years with very great abdominal distention, and an appearance entirely like that of congenital dilatation of the colon. For the relief of this the physician in charge wished to have an operation performed. The early history of the case, and, still more, the fortunate knowledge which I happened to have of the condition of the boy in his first year of life, made me oppose surgical interference on the ground that the colonic dilatation was the result of atony from prolonged digestive disturbance, i. e., *acquired* dilatation; and that with improved health the trouble would disappear. A few years later I learned that the boy was entirely well. Now, although operation might have succeeded in this case, yet it is a surgical procedure fraught with danger, and it would have been a grave mistake to have subjected the child to it. The important matter, then, in any form of dilatation is to assure ourselves that the case is really one of the congenital idiopathic class. In this event operation is the only course which can be recommended.

DR. MACHELL: The small intestine was taken off about 3 inches above the appendix. The question has been asked here if the operation is justifiable? Judging from Mr. Lane's statistics, it is justifiable. I think Mr. Lane has probably done more work for this condition than all the other surgeons combined. No other surgeon has shown such statistics. Mr. Lane did the operation in a very easy comfortable way, sitting on a high stool; he did it very rapidly, and the operation took about 2 hours. One step in the operation which interested me was the purse-string suture looped toward the pelvis, so that no kinks could occur. There was no pus, not even a particle of moisture in the skin-wound; it healed perfectly by first intention. (Intestine exhibited.)

THE RELATION OF THE PHYSICIAN TO SOCIAL SERVICE

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The realization that hospital treatment has concerned itself too closely with the illness itself without sufficient regard for the patient, the conditions which produce the illness or the permanency of its cure—together with the growing appreciation of the importance of the prevention of disease as an integral part of medicine—have resulted in the development of the art, soon to become the science, of so-called social service.

Years ago, before the present conception of such work, a beginning was made in the discharge of some of its functions through the agency of the follow-up or visiting nurse. Some physicians—and probably more hospital managers—are convinced that the educational work of the nurse in the homes of the poor constitutes all the activity which the functions of the hospital permit.

As a counterpoise to this somewhat elementary view, Richard C. Cabot—than whom no physician has devoted more careful thought to it—describes social service as the child of the poor but honest parents, "philanthropy" and "charity." He believes that the essence and center of social work, which corresponds to diagnosis and treatment in medicine, is the "study of character under adversity and of the influences which mould it for good and ill." The ultimate development of the science, therefore, would be "psychical diagnosis and treatment." Again, according to Cabot, the social worker becomes an expert in the understanding and management of the weaknesses and perversions of character, should command an expert's fees and should have his office hours and private practice, as well as his work among the poor.

In this conception the social worker remains from first to last a strictly non-medical agent.

While it is not hard to see the possible truth in this prophetic vision, the hospital, for some time at least, will furnish the greatest opportunity for the activities of social service, and the eminence of the expert in social work—as in medicine—must be attained through long years spent in the practical work of the clinic. If we are to conceive of its chief function as essentially psychologic, what becomes of the other requirements of hospital service which demand relief for material ills?

The more we study the needs of the hospital patient, the more complex become the problems, not alone of medicine, hygiene and psychology, but of sociology, of economics, of ethics, of law, of eugenics. For example, the convalescent choreic child is found to live in an overcrowded, noisy tenement, under constant hectoring by an overworked, undernourished, psychopathic mother who is struggling to bring up a family of eight on resources scarcely fit for two, and whose drunken husband's wife-beating predilections are especially manifest during her months of pregnancy—not an overdrawn picture, and yet, from a broad social standpoint the vital problems in each phase of it almost defy solution.

There will be no absolute agreement as to the best theoretical means for the prevention of such conditions. They involve too deep the great questions of the limitations and defects of human nature and of the duty of society toward its weaker members. Practical assistance must content itself with relief, so far as possible, and with preventing the recurrence of these conditions in that family group.

As a general rule, it may be stated that there is no social problem of any complexity which does not, first or last, become concerned with questions of health. In this conception of health, however, mind as well as body should be included.

Charles W. Burr recently proposes to restrict the meaning of the formal term "psychology" to "the study of how the normal brain thinks." It is clear that the study of the effects of poverty and social ills on mental processes and development constitutes a separate division of the main subject, with which sociologists are particularly concerned. It is equally clear, however, that many of these psychical-social characteristics have been known to physicians long before modern sociology even was conceived. Every trained alienist must know them before he is competent to diagnose adequately mental aberrations, and even the general practitioner acquires a practical knowledge of the mental processes of his patients, although it would be difficult or impossible for him to formulate such knowledge. With the increasing appreciation of the medical importance of psychical effects and causes, therefore, psychology and medicine can never be completely dissociated in medical-social activities!

Since disturbances of health, in its broadest sense, are such important factors in the etiology of social ills, and since hospitals, for the time at least, have extended their functions so as to embrace as many

problems of health as circumstances will permit, why is it that physicians, as a class, are not assuming greater responsibility in directing the social work of hospitals instead of leaving it largely in the hands of lay workers and lay managers? Is it because physicians have failed to grasp the basic value of this work and its direct relation to medicine? Or, after due consideration, are they convinced that the work is chiefly a sociologic measure and therefore have left to lay workers its organization, development and direction?

In order to get some light on this, in February I sent a questionnaire to members of the American Pediatric Society and other physicians interested in pediatrics. I may take this opportunity for expressing appreciation for their kind cooperation—and also for the friendly criticism and advice of Dr. H. R. M. Landis, director of the Phipps Institute, University of Pennsylvania.

Social service departments have been installed in one or more hospitals in eleven out of eighteen cities from which reports have been received. Out of sixty-nine hospitals, twenty-nine maintain more or less complete social service and nine perform follow-up work with nurses; thirty-one, or 45 per cent., apparently make no attempt at after-care, although in a number of instances this deficiency is about to be corrected. If the attempt were made to secure data on all hospitals in the United States, there is little doubt that this percentage of "deficients" would be nearer 90 than 45 per cent.

In every instance physicians approve of social service—only a few stipulating that proper management is essential to success.

The failure of so many hospitals to adopt it probably should be laid to lack of resources or to conservatism on the part of managers, rather than to lack of initiative on the part of the medical staffs.

It is of interest to note the attitude of physicians toward the records of social service investigations which can be shown in the following table:

	Social service records routinely incorporated in or added to medical histories.	Occasionally added if considered important.	Not added to medical histories but kept on file in the social service department.
House cases	5	5	13
O. P. D. cases	7	7	9
Total	12	12	22

In addition to records, the practice in most dispensaries provides that the social service nurse attend the clinics and make verbal reports. While this information enlightens the physician at the time, it must often fail to be recorded and therefore loses much of its statistical value. Nor is it sufficient for records to be on file in the social service archives, since they are not so available, and consequently will not be so frequently consulted. The social conditions of a patient as they affect health, disease and treatment should be recorded with the medical history of that case. Irrelevant records of social administration, sources of relief, etc., should be filed separately in the social service department, with the complete social record.

In order to determine the physician's conception of social work, this question was asked:

"Recognizing their close interrelationship, which do you consider the more important—the medical or the sociologic function of social service work in hospitals?"

Apparently there was some difficulty in interpreting this question. The replies were as follows:

Sociologic	22
Medical	12
Medical (for children)	1
Medical (if hygiene and sanitation are included)	1
Medical from the individual standpoint; sociologic for eliciting information	1
Equal or inseparable	7
Not comparable	1
Variable depending upon sociologic conditions	1

The balance seems to be in favor of the view that the sociologic functions are more important.

As a corollary to this we find that in many instances physicians take no active part in the general direction of social service operations. For example:

SOCIAL SERVICE DEPARTMENTS

Directed by hospital managers through head workers and superintendent, twelve hospitals.

Directed by head worker, alone or with ladies' aid societies, three hospitals.

Directed by head worker, with "cooperation of physicians," three hospitals.

Directed by physicians, head worker and superintendent, three hospitals.

Directed by executive committee consisting of representatives from board of managers, medical staff, ladies' aid societies and the head worker, 3 hospitals.

It is uncertain whether this failure of physicians to assume some of the responsibility of direction is due to disinclination or to lack of opportunity.

To sum up, the evidence shows:

1. That physicians approve heartily of social service and appreciate its value.

2. That hospitals are somewhat slow to take it up.

3. That physicians consider it more as a sociologic adjunct to, than as an integral part of, medicine.

4. Partly on this account, partly for lack of opportunity and for unknown reasons, they often fail to assume responsibility for directing it.

Let us examine more closely the questions of function and direction:

In the seventh annual report of the Social Service Department of the Massachusetts General Hospital a table is published to show a selected group of twenty-six diseases and the social treatment which they demand. This list comprises tuberculosis, typhoid, syphilis, functional nervous disease, varicose ulcers, etc.—diseases which form the bulk of the day's work at a dispensary. Of the various forms of social treatment, those which could be performed chiefly on the basis of sociologic training I have grouped as sociologic functions; those which a trained nurse could best perform, as medical functions:

SOCIOLOGIC FUNCTIONS

	Of Special Importance	Of Occasinal Importance
1. Support for patient or family	8	10
2. Help in finding or changing work	5	6
3. Persuasion, encouragement, consolation, training	4	10
Total	17	26—43

MEDICAL FUNCTIONS

	Of Special Importance	Of Occasinal Importance
1. Prevention of contagion and discovery of cases in home	4	6
2. Advice and guidance in plan and of treatment	7	11
3. Nutrition and hygiene, person and home	3	13
4. Home nursing	3	9
Total	17	39—56

The figures represent the number of diseases in which the functions were required, and show a slight preponderance in favor of medical functions. By ruling out nine adult diseases, such as cancer, to make the list more applicable to children, we find the medical preponderance even greater.

DISEASES FOUND IN CHILDREN

	Special Importance	Occasinal Importance	Total
Sociologic functions	11	18	29
Medical functions	14	29	43

Let us add to this the feeding cases of a babies' dispensary:

	Special Importance	Occasinal Importance	Total
Sociologic functions	11	20	31
Medical functions	17	29	46

In a paper before the National Conference of Charities and Correction in June, 1912, Michael M. Davis, Jr., director of the Boston Dispensary, has tentatively classified the needs of their 30,000 annual patients. Roughly, he divides them into four classes:

Type one.
Where social problem is evident and acute.

Type two.
Where social problem is not acute, but the disease is dangerous to others.

} Call for medical social case work. } 25 to 30 per cent.

Type three.
Where there are no acute social problems (poverty, ignorance or employment) but disease requires faithful attendance on the part of the patient.

} Call for social work, but mainly by clinical methods. } 40 to 50 per cent.

Type four.
Where there is no need for social service, 25 per cent.

Again, the preponderance would seem to be in favor of medical functions.

Such evidence is significant, coming as it does from institutions in which social service operations have reached a high degree of development.

I am inclined to believe that, broadly speaking, the chief functions of social service in general hospitals are medical. That this is true of children's departments or hospitals I am convinced.

For work among children the functions of social service may be defined as follows:

1. To instruct in home treatment of outpatients and to secure their regular attendance.

2. To prevent the occurrence and recurrence of disease by instructions and demonstrations in the home on hygiene, dietetics and sanitation.

3. To detect and guard against contagious disease.

4. To detect other diseases, including mental backwardness, etc., and to advise and direct their proper disposition and place of treatment.

5. To instruct in prenatal care.

All of these are strictly medical functions.

6. To secure trustworthy social data in the home and to carry out special medical-social research. The value of these investigations is just becoming appreciated.

This function is more medical than sociologic.

7. To overcome demoralization in the home by instilling hope and courage, renewing confidence, etc.

8. Conservation of resources; finding or changing employment; providing apparatus and emergency supplies; support for patient or family; moral suasion and instruction, etc. The last two require purely social work.

The amount of such social work which a children's hospital may perform will depend in part on its policy and resources, in part on the qualifications of the social worker—which suggested the following question:

"Who is the best agent to have in charge of social service departments—a graduate nurse trained in social service work or a lay social service graduate who has not had training as a hospital nurse?"

On the basis that other qualifications were equal, forty physicians preferred, without other stipulations, the trained nurse; two preferred a nurse for work among children; one preferred cooperation between nurse and lay worker; two preferred a nurse if only one worker be employed; otherwise the lay woman; one preferred the lay worker; and one believed that each worker must be judged on an individual scale only.

Undoubtedly the personal factor is of first importance—no work requires greater patience, optimism, humanitarianism, tact, judgment and, above all, common sense. The worker must know the characteristics of the people whom she is trying to help; and there is no greater cause of ineffective work than failure to appreciate their viewpoint. She must

be able to grasp the essentials of the problems and not be misled into wasting time and energy on details whose correction should be deferred or possibly not be done at all. Social rehabilitation usually should be evolutionary, not revolutionary. In addition to such qualifications, the head of the department should possess executive ability, the faculty of inspiring work, the ability to preserve harmony and, especially, mental poise. In developing such a combination of attributes education is a most important factor.

For this reason we find so many heads of social service departments among laywomen, whose educational advantages are so much better than those of the average type of the trained nurse who is, first of all, a wage-earner.

Granted the necessary personal and educational equipment, it would seem that the training in a large general hospital supplemented by sociologic training must furnish the best preparation for medical-social work. The nurse learns to know the people before she learns sociology, and, at the same time, is acquiring essential knowledge of disease and treatment. Women's colleges teach theoretical sociology, but unless the student learns to know intimately the human nature of the slums, her equipment must be as incomplete as is that of the medical student without bedside instruction. Social settlements may teach practical sociology, but both college and settlement fail to supply knowledge of disease and its treatment.

For the preference for nurses for medical-social work, therefore, there seems to be good grounds.

The amount of theoretical good which social service can accomplish is infinite. How efficiently the work is being performed in various clinics is difficult to judge. The number of cases treated and the cost per case furnishes a wholly inadequate basis for comparison. For example, I find that the lowest cost per case is 35 cents where the operation is carried on in a congested district at close range and is, presumably, follow-up work; the highest cost per case is $9.50 where the social treatment is thorough and is carried to completion. Apart from these two extremes, the average seems to be about $2.50.

From my own experience, lack of efficiency and consequent high cost per case will be due to failure to properly organize the department and to outline its plan and scope of operation and what may be called its technic. While too much system at times leads to a deadening routine, there

is no doubt that we can accomplish results with a distinct saving of time by the application of business methods in designing information blanks, collecting and recording information, filing systems, etc., and in the organization of the social service staff, disposition of workers, etc. Efficiency engineering, of which we hear so much of late, can be applied to every branch of endeavor—philanthropic as well as gainful.

It is not sufficient to carefully organize and then relinquish the entire administration to a head worker. While she may receive cooperation and advice from any of the physicians to whom she applies, the best interests of the department demand the directing services of a committee composed, preferably, of representatives of the medical staff, board of managers, and, if desirable, of the ladies' committees, with the head worker.

As Thomas B. Cooley[1] points out, "social work is becoming so popular that there is some danger of its being attempted without the skilled direction which is essential to success." "Indifference on the part of physicians and overzealousness on the part of lay philanthropists and health authorities may lead to miscarriage and waste." The need of physicians in the control of such functions as medical-social work would seem to be self-evident.

In the annual report of the well-organized social department of a prominent hospital, there may be found these sentences written by a physician: "Doctors are as untrained in social diagnosis as laymen in medical diagnosis. Put a lawyer to tuning pianos or a cook to selecting schoolteachers, and you have a parallel."

Apparently this was part of a commendatory description of social work, and was not intended as an arraignment of the doctor. Whatever its motive, in the main, its truth cannot be questioned. As a class we have been slow to recognize the importance of many of the lessons taught by sociology and have allowed our study of disease, the figure in our limelight, to blind us to much of the background out of which disease emerges.

The art of medicine of yesterday was too conservative in its conception of its true functions. So far as it has gone, the prevention of disease has proved to be one of the greatest achievements of the science of medicine of to-day. We must extend preventive principles so as to include, not only the assault of contagion, but also the less spectacular, but no less dangerous undermining of faulty habits and environment.

1. Cooley, Thomas B.: Trans. Section on Dis. Chid., Am. Med. Assn., June, 1912.

Between prevention of disease and preservation of health there is no essential difference and surely the physician and not the sociologist should become the logical arbiter of all the problems relating to health. Just as we are developing the science of public health and have supplied trained specialists to health boards, so we must be prepared to develop the science of medical sociology and its expert exponents, to whom will be intrusted the amelioration or eradication of social ills as they affect health. Social service points the way to this development, and both physicians and the general community owe a large debt of gratitude to the pioneers in medical-social work.

The evolution of the new type of sociologic physician should be by and through the activities of social service. He will have received some training in sociology and its allied branches before taking up his medical studies. In the medical school he will devote much more time to hygiene, psychology and eugenics than is at present allotted to them. After his hospital service, by postgraduate work he will equip himself more thoroughly in these branches and in sociology and will then be sufficiently expert to be placed in charge of hospital social service at salary. His workers will be men as well as women—for the problems of sociology as they apply to men have, as yet, received no adequate attention. By virtue of his medical training he will be able to effect economy of time and effort. Much of the work of social service as at present organized is probably wasted because of the inability of even a nurse to discriminate and pass judgment on medical problems. For these, he will be on the court of first resort—and the journey to other courts will, quite frequently, be rendered unnecessary. At the same time his broad preliminary education and his special sociologic training, will safeguard him from the mistake of narrow vision which handicaps the student of disease *per se*.

Surely, such organization and administrative procedure will develop hospital social service to the highest degree of effectiveness.

On the other hand, I do not believe that the hospital ultimately will prove to be the logical agent for the constructive work of medical sociology. On the community itself must devolve public relief and education, the germs of which we see in social service.

And thus, again, private philanthropy will point the way to public duties.

The agent of the community must be its health department, whose guiding hand would be that of the medical sociologist. This health department of the future must extend its functions so as to include every activity which concerns the health of the community—most of which are now attempted by private agencies. Backed by the authority of the law, the health officer's powers of correction and readjustment would be infinitely greater than those of unofficial philanthropy.[2]

3942 Chestnut Street.

DISCUSSION

DR. TALBOT: Our clinic at the Massachusetts General Hospital used the Social Service Workers three years ago by sending patients down stairs to the Social Service Department. These cases were followed up and investigated after they had been treated at the clinic. Recently the social service deputed to the Children's Department, moved up stairs and were given desks in our clinic. They are now working side by side with our house officer. They do their morning work in the clinic, and in the afternoon they visit in the homes. We have come to the point where we cannot do without the social worker, and our work has doubled in efficiency. The Massachusetts General Hospital of its own accord has instituted a branch of general nursing with six months' training in social service work. This is a very popular division of the nurses' training.

DR. CHURCHILL: I agree with Dr. Gittings in that we as physicians have made a mistake in not taking a more active part, in fact in not taking the lead, in social service work. I am glad, however, to see that the physicians are beginning to realize the importance of social service work, for it is all preventive medicine, and as pediatricians we ought to take an active interest in it. The Social Service Department is well organized in the Children's Memorial Hospital of Chicago, and like Dr. Talbot, I now feel that we could not get along without the social worker. In our Hospital our babies seldom have a second stay in the hospital for the simple reason that every baby discharged is followed up by the social worker and the mother is instructed in the care of the baby; in that direction alone the establishment of the Social Service Department has justified itself. Among the older children, too, we get good results in having the social worker show the mother as to the proper care of the child; but it is not as striking as it is in the baby service.

We have a school of Civics and Philanthropy in Chicago where people are trained in all branches of social service work. They utilize for field work our hospital clinic. We have several students from that school who go out with our social workers, as assistants; in that way we are coöperating with other agencies in the city of Chicago.

DR. GITTINGS: I first became interested in this subject while serving as chairman of a committee which investigated the social service operation in one of the Philadelphia hospitals. This investigation necessitated a careful study

2. Since this paper was written the article by A. R. Warner (*Jour. Am. Med. Assn.*, March 8, 1913, p. 738) first came to the author's attention. For the past year the dispensary and Social Service Department of the Lakeside Hospital, Cleveland, have been in satisfactory operation under the executive control of a medical director.

of conditions in Philadelphia, which I followed up by this general inquiry covered by the questionnaire. I have found that physicians have a lively theoretical interest in the social service movement but that as a rule, they trouble themselves very little with its practical management and direction, or even with its results. It is hard to understand this attitude unless they consider it solely as a sociologic measure, hence beyond their jurisdiction. With this view I do not agree and believe that medical-social work will eventually prove to be as much a part of medicine as are the activities of the municipal, state and national health boards at present.

A CASE OF BILATERAL HYDRO-URETER—CHRONIC PYOCYANEUS INFECTION *

HENRY HEIMAN, M.D.
NEW YORK

N. B., male child, 5 years of age, born in the United States, admitted to the children's ward during my summer service at Mt. Sinai Hospital on July 21, 1911, with the following history: Four months ago he suddenly became ill with fever, headache and vomiting. A few days later blood appeared in the urine and stools. Pain and tenderness in the right lumbar region appeared soon thereafter. The patient has been in bed since the onset of the illness and has gradually become worse in spite of all medical treatment.

The family history was negative.

The patient was born at full term, was breast-fed for one year and then given adult diet. He has always been pale and delicate. For several years the patient has suffered from prolapse of the rectum and occasional appearance of blood in the feces.

Physical examination revealed nothing abnormal, with the exception of slight dulness in the left interscapular region and a few fine râles in the left axilla.

July 23: Von Pirquet reaction negative.

July 27: General condition good. The temperature has been normal since admission. Deep tenderness in right upper abdomen. The urine contains many pus cells, but no red blood-cells. No blood in the stools.

July 29: Urine and stools show the presence of *Bacillus pyocyaneus*.

August 4: Blood-culture negative.

August 5:

Erythrocytes	3,600,000	
Hemoglobin	47	per cent.
Index	0.7	
Leukocytes	16,800	
Differential Count:		
Polynuclears	70	per cent.
Small lymphocytes	25	per cent.
Large lymphocytes	5	per cent.

* From the Children's Service of Dr. Koplik, Mt. Sinai Hospital, New York.

August 8: Bladder catheterized and irrigated. The catheter was allowed to remain in place so as to observe whether the immediately succeeding urine is turbid. This was the case.

Aug. 13, 1911:

	Blood count 1 hour before injection of pyocyaneus vaccine.	Blood count 1 hour after injection of pyocyaneus vaccine.
Leukocytes	9,000	9,600
Differential Count:		
Polynuclears	58 per cent.	51 per cent.
Small lymphocytes	35 per cent.	43 per cent.
Large lymphocytes	3 per cent.	3 per cent.
Eosinophils	4 per cent.	3 per cent.

August 16: Cystoscopy and ureteral catheterization: Mouth of right ureter slit-shaped. Left ureter has rigid walls, is circular, golf-ball hole. Purulent urine is seen to come from the left ureter. The discharge from the right ureter cannot be seen clearly. Indigo-carmin injection negative on both sides for forty-five minutes. The bladder mucosa is normal. therefore the pyuria must be of supravesical origin.

Catheterization of ureters with No. 4 F. catheter: On right side obstruction met 1 inch from bladder; on left side, catheter passed 2½ inches.

Specimens of urine obtained from each:

URINE FROM LEFT URETER.	URINE FROM RIGHT URETER.
Urea. 0.2 per cent.	Clear.
Many pus cells.	
No tubercle bacilli.	
No growth on culture media.	

September 1, 2, 3, 4, 8: Examination of urine shows no tubercle bacilli.

September 8: General condition good. Temperature shows daily elevation to 99 or 100 F. Urine less purulent. The treatment consisted chiefly of autogenous vaccines, which were administered as follows:

August	5— 50,000,000
August	14— 50,000,000
August	22—100,000,000
September	4—150,000,000
September	10—175,000,000

September 18: Discharged apparently well.

Patient was readmitted to hospital on Aug. 12, 1912, with the history that the urine had been cloudy for the last six months, but without

hematuria. No pain on micturition. Patient has three or four watery movements each day, which at times contain mucus and blood. On physical examination nothing abnormal was found.

August 19: Urine contains many pus cells; bacteriologic examination shows the presence of *Bacillus pyocyaneus*.

September 2: No change in condition of urine.

September 24: Much pus in urine.

October 1: Examination of bladder made by Dr. Leo Buerger, to whose careful cystoscopic studies is due the first recognition of the condition of the ureters. The bladder showed a moderate degree of diffuse cystitis. What was more remarkable was the patulous condition of both ureteral orifices. The left orifice was enormously dilated, resembling the mouth of a small diverticulum. The right ureter was also enlarged, although it still retained some of the natural outline of a normal orifice. From these appearances the presumptive diagnosis of hydro-ureter and possibly also dilatation of the pelvis of both kidneys was made. He advised the use of argyrol, as in cases of relaxation of the ureters. Argyrol, when injected in the bladder, readily finds its way into the ureter and kidney, where it can be detected by radiography. Accordingly, on Oct. 7, 1912, 10 per cent. argyrol was instilled in the bladder, the patient was put in the Trendelenburg position and a Roentgen-ray picture taken. Unfortunately, but little of the argyrol passed into the ureters, and consequently only an outline of the bladder, together with the dilated lower ends of both ureters, could be recognized in the plate.

On October 18, 75 c.c. of a 20 per cent. solution of argyrol freshly prepared was again injected into the bladder and most excellent plates obtained. Immediately after exposure the bladder was thoroughly irrigated, so that no untoward symptoms followed from the use of this strong solution. Indeed, the urine became clearer and the number of pus cells greatly diminished.

The plate (Fig. 1) shows the shadow of the bladder, the right ureter somewhat less distinct than the left.

A week later 40 per cent, argyrol was injected and the picture in Figure 2 was obtained. For some unexplained reason the argyrol failed to show in the right ureter, but the outline of the left ureter, its tortuous course and the peculiar shape of the left renal pelvis is strikingly shown.

Considerable distention of the bladder was found on cystoscopy; at one time it held as much as 300 c.c. of urine. No obstruction was found,

either by the cystoscope (caliber 12 Fr.) or by a silk catheter (14 Fr.) by means of which the argyrol was injected. So that although there was no urethral obstruction to the passage of a rigid or flexible instrument, there was present, nevertheless, a considerable degree of urinary retention.

The etiology of the ureteral dilatation is not easy to determine in this case. According to Coustere (*Paris Thèse,* 1910), there are two kinds

Fig. 1. Showing only bladder and dilated lower ends of ureters.

of hydro-ureter — congenital and acquired. The causes of congenital hydro-ureter are as follows:

A. Obstruction at the vesical orifice:

1. Imperforate vesical orifice, occurring either with a single or double ureter.

2. Stricture of the vesical orifice with or without prolapse of the ureter in the bladder.

3. Normal opening into the bladder associated with stricture.

4. Diverticulum of the ureter compressing the normal ureter.

B. Obstruction along the course of the ureter, either in the form of a stricture, valve, kink or twist.

Fig. 2.—Showing markedly the left ureter and dilated left renal pelvis.

Acquired hydro-ureter may be divided into three classes:

1. Hydro-ureter due to obstruction outside the ureter.

2. Hydro-ureter due to obstruction situated in the wall of the ureter.

3. Hydro-ureter produced by an obstruction in the lumen of the ureter.

Again, the assumption that we are here dealing with the congenital variety is the fact that there is no demonstrable atresia, stricture, valve, kink or twist. If acquired in Nature, it could certainly not have been caused by an obstacle outside of the ureter, for in this child with thin abdominal walls, anything compressing both ureters could easily have been felt if present. Nor is it probable that the obstruction was situated in the walls or lumina of the ureters.

Two other possibilities must be entertained: 1. A paralytic condition of the bladder due to a local poliomyelitis affecting the segment of the cord innervating the detrusor muscle. 2. An obstacle in the urethra which prevented a thorough emptying of the bladder.

As far as could be determined, there was no history of an attack of poliomyelitis, nor were there any other evidences of a nerve lesion. Although the possibility of a urethral obstruction could not be ruled out, it was not such as to prevent the passage of a moderate size catheter.

We assume that the following conditions may obtain: First, that we are dealing with a case of dilatation of the ureters and pelves of the kidneys of anomalous origin; or, second, with an acquired type of hydroureter due either to a paralytic condition of the bladder or to an obstruction of the urethra that interferes with the outflow without preventing the entrance of a catheter. At any rate, the unusual findings and the mode by which the diagnosis was established are of sufficient interest to warrant our putting the case on record. Of interest, also, is the fact that, although temporary improvement resulted from the use of pyocyaneus vaccines, results of permanent value could not be obtained by this mode of treatment.

DISCUSSION

DR. J. D. LOVE (Guest): I should like to inquire what position the patient assumes when the instrument is inserted into the bladder?

DR. HEIMAN: The child is inclined, and placed in the Trendelenberg position. One should not speak of these cases merely as pyelitis, that is ordinary pyelitis, but we ought to determine the causative agent of the infection. The majority of cases have been called colicystitis. In other cases various bacilli or streptococci have been found, and one should indicate which organism is responsible in producing the condition.

CASES OF EDEMA IN INFANTS

HENRY DWIGHT CHAPIN, M.D.
NEW YORK

It has long been known that local and general edemas, not due to nephritis, are occasionally seen in early life, but the causes of this condition have been variously explained. It may thus be of interest to report a series of cases in which various symptoms were noted and studied in their relation to the edema. As some of these cases were accompanied by slight albuminuria, it may be well to recall that any marked bodily disturbance in the infant is apt to show some abnormalities in the urinary findings, such as occasional traces of albumin and even a few hyalin casts.

Some years ago the writer reported examinations of the urine in eighty-six cases of mild and severe gastro-intestinal disturbance, and small amounts of albumin were found in seventy-five of them; and in a series of fifty-seven cases of pulmonary disease, traces of albumin were noted in forty-nine. Other observers have called attention to the same condition. This cannot predicate the presence of actual renal disease, but, rather, an irritation of the renal tubules accompanying a slight congestion and having no special significance. Attention is here called to this fact, in order to emphasize the point that edema in infants is not to be considered as due to nephritis simply because small amounts of albumin are found in the urine.

We must try to differentiate a little more in this class of cases. It will doubtless be found that the causes are often complex and due to a combination of a number of abnormal conditions.

A clinical study of twenty-one cases gave the following data:

Age of Patients.—One, 16 days; two, 5 weeks; one, 7 weeks; one, 2 months; three, 3 months; one, 3½ months; two, 4 months; two, 6 months; two, 8 months; two, 1 year; two 2 years; two, 3 years.

Condition of Infants.—One was premature, twelve had malnutrition with digestive troubles, two were apparently healthy, two had bronchopneumonia, one had pericarditis with effusion, two had otitis media and one had cerebrospinal meningitis.

Location of Edema.—In four it was general, two of which were preceded by a maculopapular rash; in seven the ankles and feet were involved, two had involvement of the face only, in one the right knee, left hand and left forearm were affected, in two both feet and hands, in one both wrists, in two the face and both feet, in one the face and abdomen, and in one the scrotum and penis.

Blood Examinations.—In twelve cases the blood was examined, six of which showed mild, secondary anemia, with differential counts right. Three showed normal, or high red, blood-count, 5,800,000, 6,800,000, 5,000,000. In no case examined was there any evidence of pernicious or profound anemia, except, possibly, one that gave a very poor showing, that is, reds, 1,900,000; hemoglobin, 85 per cent.; whites, polymorphonuclears, 48 per cent., and lymphocytes, 52 per cent. However, there were no nucleated reds, megalocytes or microcytes and no poikilocytosis. The examination in these cases showed no more blood disturbance than in similar types of illness without edema.

Condition of Stools.—Twelve were abnormal, seven were fair and two unaccounted for.

Condition of Urine.—In nineteen cases the urine was examined with the following results: Albumin was present in faint traces in nine cases and heavy trace in one case. It was absent in nine cases, and sugar was not found in any of the specimens. Seven of the specimens examined showed occasional casts, five of them hyaline and granular, and two with hyaline casts. The rest of the examinations never showed even occasional casts of any kind. One case showed pus and one had the phenolsulphonephthalein test applied with 55 per cent. return, although there was a slight leakage.

Weight of Infants.—Three gained in weight while under observation, eight remained stationary, eight lost in weight, and in two the weight was not noted.

The duration of the edema in these cases varied from three to twenty-one days. There were seven deaths, three from malnutrition, two from bronchopneumonia, one from cerebrospinal meningitis and one from pericarditis with effusion.

A few individual cases will be cited as fairly typical of the series:

CASE 1.—Healthy baby of sixteen days. Weight, seven pounds, eleven ounces. Swelling of the left hand and forearm and right knee. Baby was in hospital for fifteen days, and the condition remained unchanged on discharge. The blood

showed hemoglobin, 85 per cent.; reds, 5,800,000; whites, 14,600; polymorphonuclears, 53 per cent.; lymphocytes, 47 per cent.; Wassermann negative. The urine showed no albumin, casts nor sugar. Half an ounce of fluid was obtained from the right knee by aspiration, which showed no growth culturally. Guinea-pig injected and lived.

CASE 2.—Premature baby of seven and one-half weeks. Weight, three pounds fourteen ounces. Edema general, preceded by maculopapular rash. Duration, six days. Stools frequent, green and watery. Blood showed marked anemia of the secondary type. Three examinations of urine were made during the attack, showing faint traces of albumin and a few hyaline casts. The baby left the hospital in good condition, with urine normal.

CASE 3.—Pericarditis with effusion in a baby of two years. Edema started in both feet, lasting, off and on, for three weeks. Before death, the edema affected the face, but no other part. The temperature was high and irregular, and the stools loose and frequent. Two examinations of the blood were made. (1) Hemoglobin, 75 per cent.; reds, 4,000,000; whites, 26,000; polymorphonuclears, 75 per cent. (2) Hemoglobin, 64 per cent.; reds, 3,800,000; whites, 16,000. A culture of the blood showed pneumococci. The urine showed traces of albumin, with hyaline and granular casts. Later on the results of the urinary examinations were negative. The baby died from exhaustion.

In a study of these twenty-one cases, it seems that neither the condition of the blood nor urine can satisfactorily explain the edema. While the exact cause, or causes, may be obscure in a given case, I believe, in the present state of our knowledge, we can make a rough classification of the kind of cases that are apt to show this phenomenon.

1. Difficult digestion and malassimilation. Diarrhea can produce toxins that may induce vasomotor paralysis. Twelve of my cases had intestinal disturbances, shown by abnormal stools. Dr. W. E. Hume[1] has reported thirteen cases in which general edema followed gastro-enteritis in infants and young children. Neither albumin nor tube casts were found in the urine in any case. In eight of the cases in which the blood was examined, some degree of secondary anemia was found. Two of the patients died, and both showed abnormal fibrosis in the suprarenal glands, and the author suggests future study of these glands in this connection. Another theory is that the condition may be due to retention of salts in the tissues, particularly sodium chlorid and the phosphates, but Hume, in observations on two normal cases and two of edema, failed to discover any difference between the salt exchange in patients suffering from this variety of edema and that which takes place in perfectly normal children. These edemas, with intestinal disturbances, are probably somewhat analogous to the urticarias.

1. Hume, W. E.: Brit. Med. Jour., Sept. 2, 1911.

2. Edema is seen in various exhaustive conditions, such as prematurity, marasmus, extreme secondary anemias, edema neonatorum and in long debilitating diseases.

3. In various constitutional diseases, such as syphilis, tuberculosis, erysipelas, pertussis, etc., edema is an occasional accompaniment.

4. Angioneuroses of vasomotor origin will explain the phenomenon in certain instances. Two of my patients were evidently of this nature.

It would seem as if the kind of edema here described would form an interesting subject for future and collective study.

DISCUSSION

DR. HAND: I should like to express my agreement with Dr. Chapin. All the cases I have seen have had digestive disturbances.

DR. LA FÉTRA: I have seen quite a number of these cases of edema following digestive disturbances, and most of these patients were found to have been on a very thin diet, such as barley water, and I feel convinced that the dilute carbohydrate food is the cause of the edema. In my experience it seemed to be a lack of proteids in the food that brings about the anemia and the edema; because when a reasonable dilution of milk, or skimmed milk or *Eiweissmilch* is substituted, the edema disappears rapidly. I have seen fewer of these cases of edema since *Eiweissmilch* has come into use. This is probably because the *Eiweissmilch* has a high proteid content.

DR. NICOLL: I should like to ask Dr. Chapin if he thinks it correct to classify two of these cases under the head of idiopathic edema, since there were present unmistakable signs of local infection?

DR. BLACKADER: I have had a few cases of gastro-enteric diseases in which edema was a late symptom, and they seemed to me to be due to a deficiency in proteid feeding, and I found that generally some increase in the proteid did good. There was, however, a definite mortality among them. Edema coming on late in gastro-intestinal disease is a dangerous symptom. In my practice—speaking from memory only—I have seen seven or eight cases.

DR. MCCLANAHAN: Recently I saw a case of a child that had edema at 6 months of age. I was called in by the dermatologist. It had been on a diet of rice water for 10 consecutive days without any milk. The hemoglobin was 60 per cent. and I think the edema was due to secondary anemia. The child was placed on an increased diet and the condition cleared up and the urine showed no albumen. Where the edema is due to starvation a heavier diet will usually clear up the condition. This case I have cited certainly seemed due to that cause.

DR. MACHELL: Three or four summers ago I saw six babies (in consultation) with this edema. Only one had casts in the urine and that baby died. They were all feeding cases and all the others got well on change of diet. The disease is a summer one and though a physician does not see a great number of these cases, they are practically all feeding cases. The majority of them get better on a rearrangement of the diet.

DR. TALBOT: The knowledge of the salt metabolism up to date is very small, and therefore is not well understood. It is probable that the answer as to the

etiology of edemas will not be forthcoming for many years. After the normal metabolism is understood, it will be possible to say what is pathological. The salt metabolism is so mixed up with the metabolism of other food constituents that it is difficult to say which element in the food is the cause of the symptoms or how much the relation of it to the other food components will influence its action. Sodium chlorid in large doses may be dangerous to the infant because it may cause sudden edema of the lungs.

DR. CHAPIN: My object in reporting these twenty-one cases was to clear up in my own mind certain causes. I believe in these cases the blood and kidneys had nothing to do with the condition. It does seem that it is a warning of a terminal condition and may thus serve as one indication of a fatal outcome. In a number of cases it was due to starvation for when a regulation of feeding was instituted they gained in weight under feeding by proteid. I believe it is often due to a condition of exhaustion and to something else as well. As Dr. Talbot says, it will be many years before we understand the condition thoroughly, and until we do understand it better we must not use salt carelessly, but we must watch for the symptoms of this condition and if they appear we must feed up our babies and support them in every way possible.

DESCRIPTION OF A MODIFIED MACKENZIE INK POLYGRAPH

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The records obtained by sphygmograph tracings are liable to many variations, particularly in children. These variations are dependent on the instrument, the movement of the arm at the time of making the sphygmogram and the personal equation incident to the operator. Not all of these factors can be eliminated entirely, but by using a sensitive tambour, enlarging the roll and changing the surface of the paper the excursion of the pen records more accurately and lessens the errors. Smoked paper is replaced in the apparatus here illustrated by smooth paper that takes ink readily and the recording pens are made larger than the capillary tubes favored by Mackenzie.

The error incident to the movement of the arm is lessened by making use of the carrying box of the polygraph for a rest. The personal equation of the operator can be overcome only by experience and by remaking polygrams under the same, or as nearly as possible under the same conditions. The modified Mackenzie ink polygraph has advantages over the original Mackenzie instrument in the width of the paper, the three tambours and the recording pens.

With three tambours, the radial, cardiac and carotid or jugular pulsations may be recorded simultaneously and comparisons made of the cardiac and vascular tracings.

Like all instruments of this character it is not exact, but it leads to exactness and should be used whenever possible in studying cardiac and vascular diseases.

Description.—The body, A. (Fig. 1), contains the paper roll and time markers. The writing tambours BBB with supporting bar B.[1] Wrist tambour C, with attachement C[1] for strapping on to wrist. Paper roll bracket D. Paper roll D.[1] Pens FFF and time marking Pen F.[1] There are three keys. The large one (1) is for winding the paper rolling movement, the top smaller stud key (2) for winding time marker movement, and the bottom one (3) regulates the speed of the paper passing through the rollers, the direction required being indicated by F and S (fast and slow). On the top are the writing table (4), friction rollers and tension spring (5) for passing along the paper. Behind these, to the right, is the start and stop lever (6) and to the left the fork (7) carrying the time

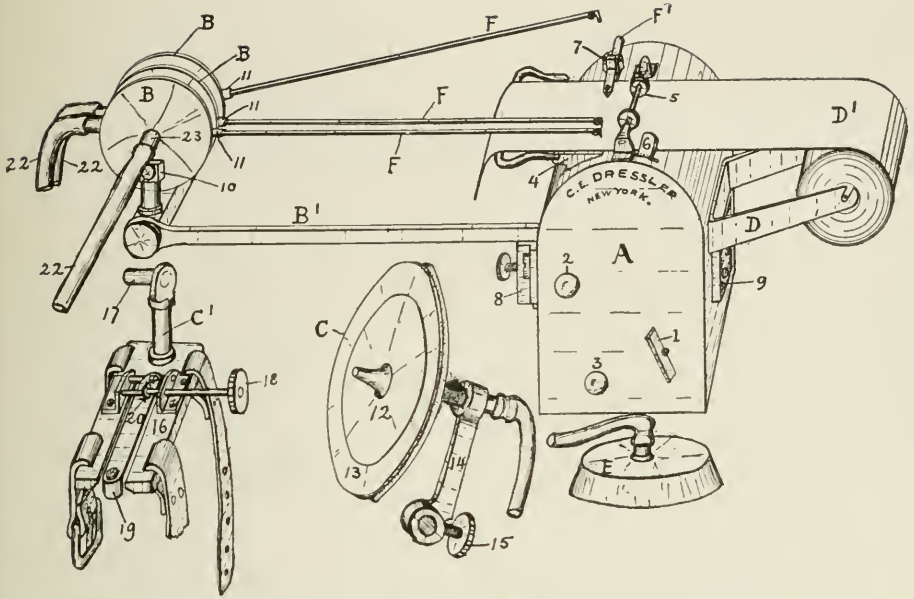

Fig. 1.—Diagram of the Modified McKenzie Ink Polygraph.

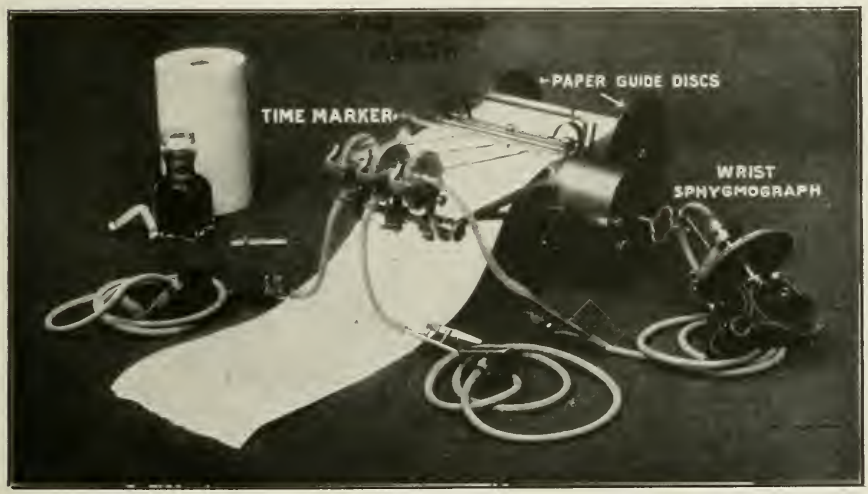

Fig. 2.—The Modified Mackenzie Ink Polygraph.

marker pen F.[1] This fork vibrates at the rate of 300 per minute (one-fifth of a second).

The square socket in front (8) holds the supporting bar of the writing tambours, while the other one behind (9) supports the paper roll basket. The writing tambours with their pen levers (11) are fitted with friction joints (10) enabling the pens to be adjusted to any desired position; micrometer screws are provided for fine adjustments. The pen levers have each a small spring at the end which presses on and holds the pens in the grooves cut out to receive them. The tambours have inlets (23) for attaching connecting tubes (22).

The wrist tambour C is in two parts: First, the splint (16), which is strapped on the wrist, is fitted with spring tongue and button (19) that rises and falls with the action of the pulse. Also an eccentric (20) and regulating screw (18) for increasing the resistance on the artery. Second, the tambour with supporting arm (14), rubber membrane (13) and compression disc and peg (12). This portion is not placed in position until the artery has been correctly located and the maximum movement of the springs and pulse button obtained. The two parts are held together by the clamping screw (15) in the supporting arm binding on to the pillar (17). The tambour itself is also secured by a binding screw.

The paper roll bracket D has a roller running in slots at the ends of the bracket arms. The roller is thus kept in position and the paper roll fits loosely on it, two larke disks guide the paper.

The receivers EE are shallow, open cups with a nipple passing out of the roof, to which an India rubber tube is attached, the other end of the tube being attached to the tambour with the writing levers. When placed over any pulsating part in such a manner that no communication is made with the outer air, the movement within the receiver is conveyed to the tambour and writing lever.

THREE TYPES OF OCCLUSION OF THE ESOPHAGUS IN EARLY LIFE *

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BOSTON

The following cases of occlusion of the esophagus of non-traumatic origin have been under my care in the wards of the Children's Hospital. The rather unusual occurrence of the condition in my experience and the importance of recognizing which type we are dealing with, on account of prognosis and treatment, are my reasons for reporting them. Considering the rarity of the condition it is to be noted as a coincidence that during Dr. Morse's service, preceding mine, three cases of esophageal narrowing entered the same wards and have been reported by him.

Case 1.—The first case is that of a boy 25 months old. The labor was normal and the infant was normally developed. He was fed on breast milk for the first seventeen months. From birth he had always vomited, from four to six times daily. The vomiting had always occurred during the feedings and was never forcible. The child gagged or coughed a little and a considerable amount of the feeding would come out of his mouth. Sometimes he vomited just as he began his feeding and the amount then was a great deal more than he had just swallowed. The vomitus consisted of unchanged milk, not curdled or sour, and had no regular relation to the feedings. Sometimes he would retain several feedings and then vomit during the next two or three. He not only vomited breast milk but modifications of cow's milk. He seemed to be always hungry and had to be fed at least twelve times a day. It was found that he vomited less if he had only three ounces given at a feeding. He had always been constipated and he soon became a pale, thin baby.

Physical examination, beginning with the mouth and throat, was negative except for the heart, which was found to be decidedly dislocated to the right, and there was a blowing, systolic murmur, loudest at the base and transmitted to the left axilla. There was no systolic retraction. The urine was normal. Listening with a stethoscope over the epigastrium, when the child was swallowing, a slight splashing sound was heard fifteen to twenty seconds after the mouthful of milk had been swallowed. The sound was like that of a metallic trickling as though the milk came into the stomach by drops. The usual time for liquid to pass into the stomach at this age is five seconds.

A bismuth meal was given and a Roentgen examination immediately made. This showed a narrowing of the lower third of the esophagus extending not quite to the cardia. The esophagus was shown to be a little to the right of the median line and there appeared to be pericardial and mediastinal adhesions. The esophagoscope showed a stricture of the esophagus about 17 cm. from the incisor teeth, approached by a funnel-shaped narrowing while the upper part of the esophagus was found to be slightly dilated. The narrowing appeared very great

and a sound, ¼ cm. in diameter, could not be introduced. It may be said here that the distance from the gums to the cardia in the newborn is about 17 cm. and at three years from 23 to 24 cm. Figures 1, 2 and 3 show the stricture and 2 and 3 show that a certain amount of the bismuth meal had trickled through into the stomach. The child lost rapidly in weight and strength and the stricture was so small that it was deemed dangerous and therefore inadvisable by Dr. D. Crosby Greene to attempt to dilate it through the esophagoscope by the usual means. I might say in passing that in congenital cases, of which type this seemed to be, there is apt to be increased connective tissue around the esophagus which may extend down and form adhesions and thus displace the heart. It was these adhesions which were supposed to have caused the dislocation of the heart to the right. The only means of saving the child's life appeared to be a gastrectomy which would permit of the child's being fed directly into the stomach, and it was thought that when the general condition improved he might be able to stand the manipulation necessary to dilate the esophagus. The operation was performed but the child died. No autopsy was permitted.

This case represents an extreme congenital organic condition of a type which as a rule is inoperable and is almost universally fatal.

CASE 2.—The second case is a more favorable type for treatment and for life. This case represents a type of probable congenital narrowing not necessarily, however, of organic lesion in the esophagus but caused by congenital central spasm, resulting in dilatation of the esophagus above the point of narrowing. A girl of 10 years old, normal at birth, was fed on breast milk for eleven months and during this time was well and strong. She was then given cow's milk and cereals and at once began to vomit regularly during her meals. She would vomit several times while taking her food. The amount vomited was small, never more than a few mouthfuls. The vomiting caused her a good deal of effort and distress until she learned to aid its occurence by putting her fingers down her throat. This continued until she was 4 years old and she had become a thin, pale, constipated child. At this time she swallowed a piece of meat in her soup and for four days following she vomited everything, even water. The vomiting then gradually lessened and she was kept on a diet of milk and cereals for two years. Since that time she had developed well and had become a strong, well girl. There was no history of her having swallowed anything corrosive. Four days before she was seen at the hospital she ate an orange and an hour later she was unable to eat her dinner because of discomfort which was only relieved by inducing vomiting with her fingers. She was unable to swallow anything, even water, without having to vomit it directly. She was in a very weak condition.

Nothing abnormal was found on physical examination. A bismuth meal was given and a Roentgen picture showed that the bismuth had passed only a little way beyond the middle of the esophagus, as shown in Fig. 4, and that there was none in the stomach. The part of the esophagus containing the bismuth was shown to be greatly dilated and at the bottom of this dilatation a circular object was made out the size of a small coin. An oval esophagoscope 1½ by 1 inch in diameter was passed into the esophagus by Dr. Greene and encountered a mass of orange pulp mixed with the bismuth. This was withdrawn and was found to be practically the whole of an orange pulp. Entangled in it was a penny. After removal of the obstruction the esophagus was examined. Marked dilatation of the lower third was observed, and a constriction ½ cm. in diameter at a distance

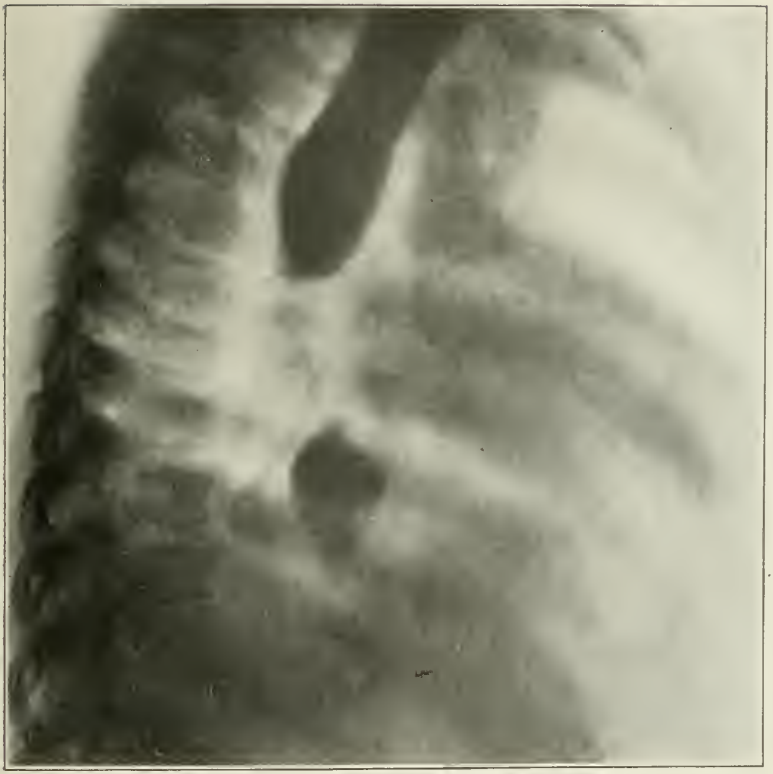

Fig. 1.—Stricture of the esophagus.

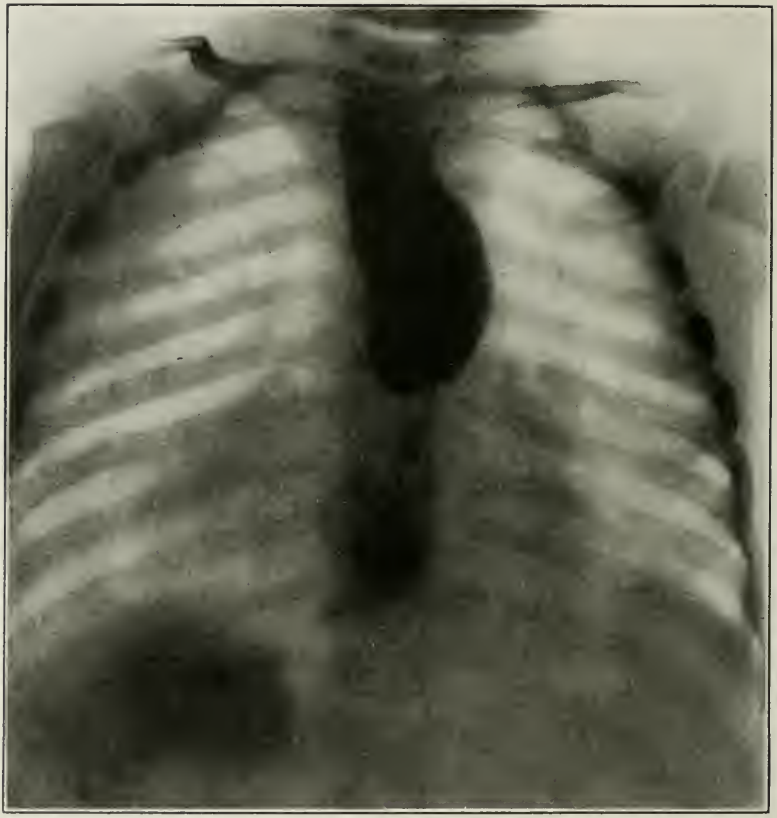

Fig. 2.—Stricture of the esophagus showing that a portion of the bismuth meal had trickled through the stricture into the stomach.

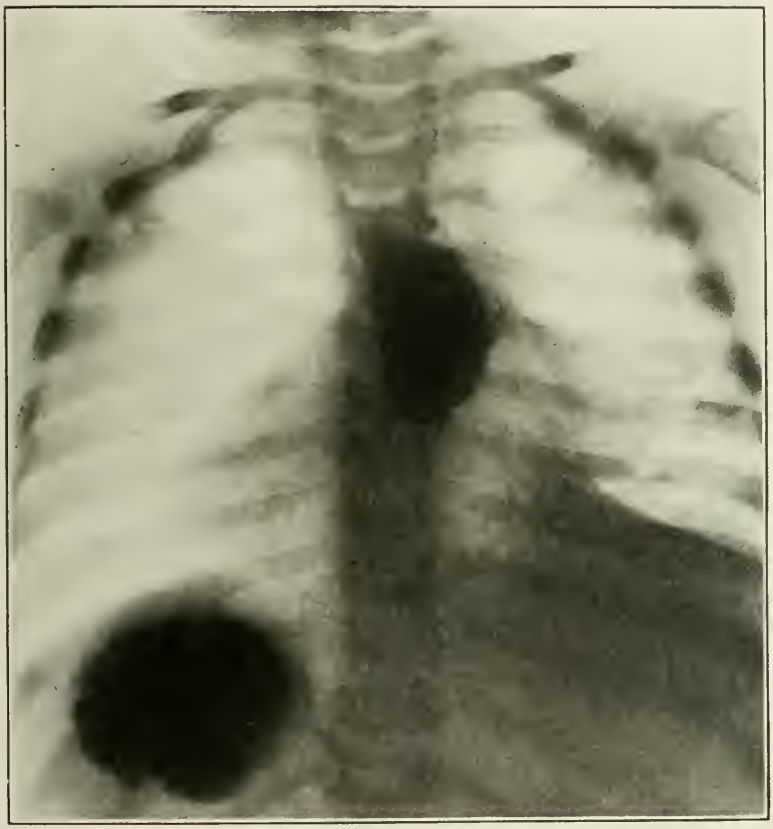

Fig. 3.—Stricture of the esophagus. A portion of the bismuth meal has trickled through into the stomach.

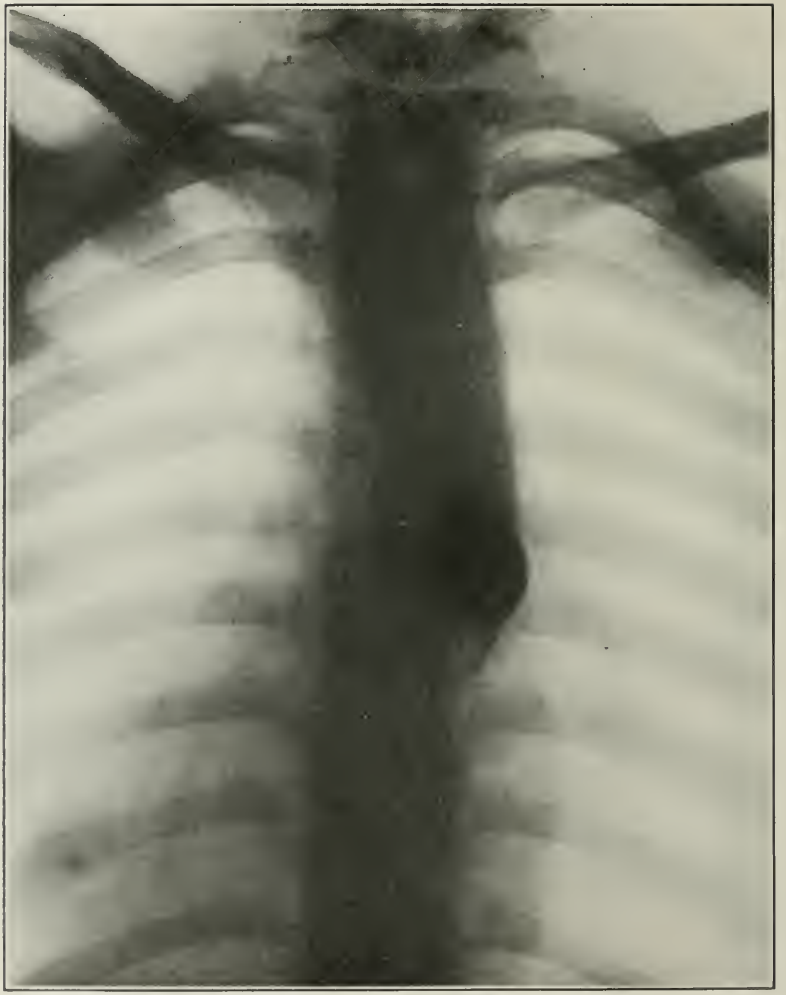

Fig. 4.—Stricture of the esophagus in a girl 10 years old, showing that the bismuth has passed only a little way beyond the middle of the esophagus.

Fig. 5.—Stricture in same case as Figure 4 after obstruction in the form of orange pulp and a penny had been removed and dilatation performed.

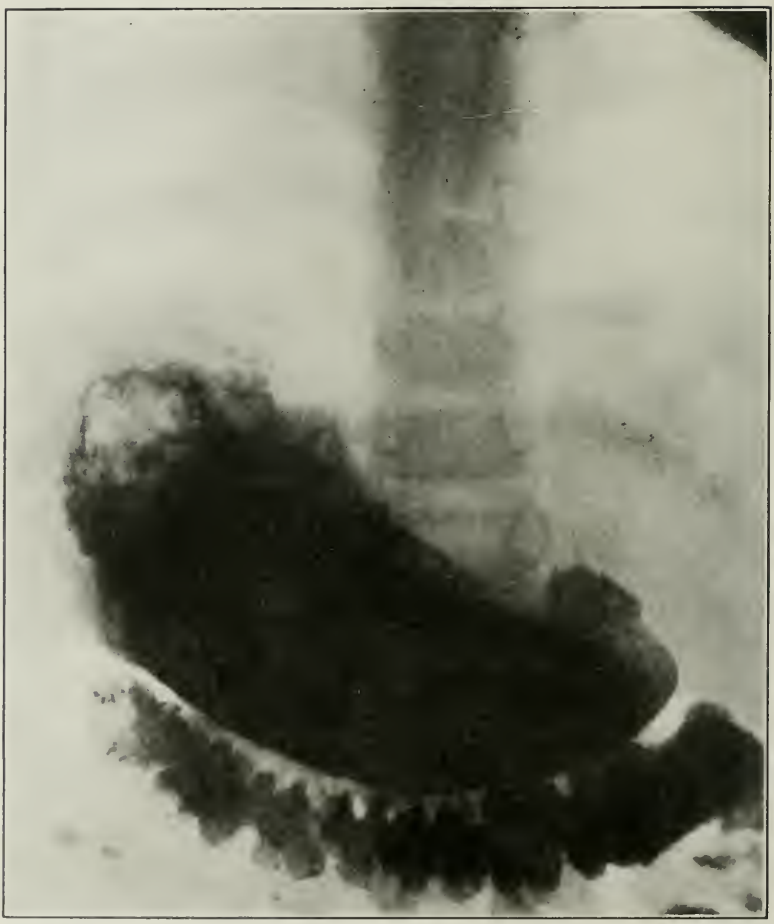

Fig. 6.—Stricture of the esophagus of the spastic variety in a boy 5¾ years old. The bismuth is shown as having passed into the stomach. There was no pyloric stenosis.

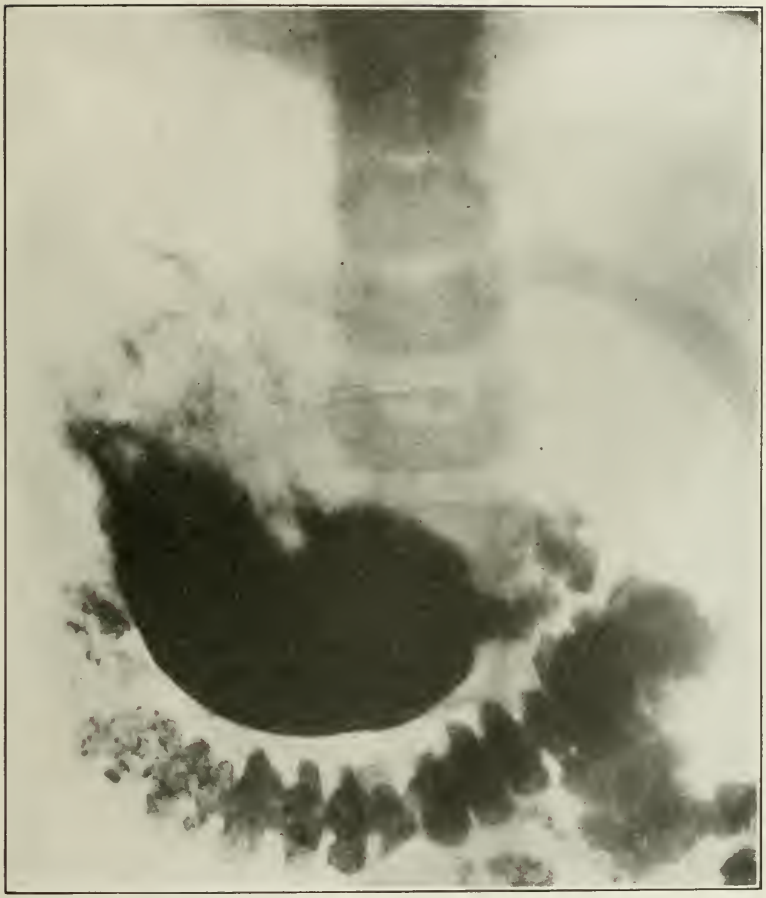

Fig. 7.—See Fig. 6 for description.

Fig. 8.—Showing the stomach tube in the stomach after brief resistance at the cardia. Same case as Figures 6 and 7.

Fig. 9.—Same case as Figures 6, 7 and 8, the child lying on his face, the esophagus full of bismuth and the presence of a stricture in the cardiac end of the stomach.

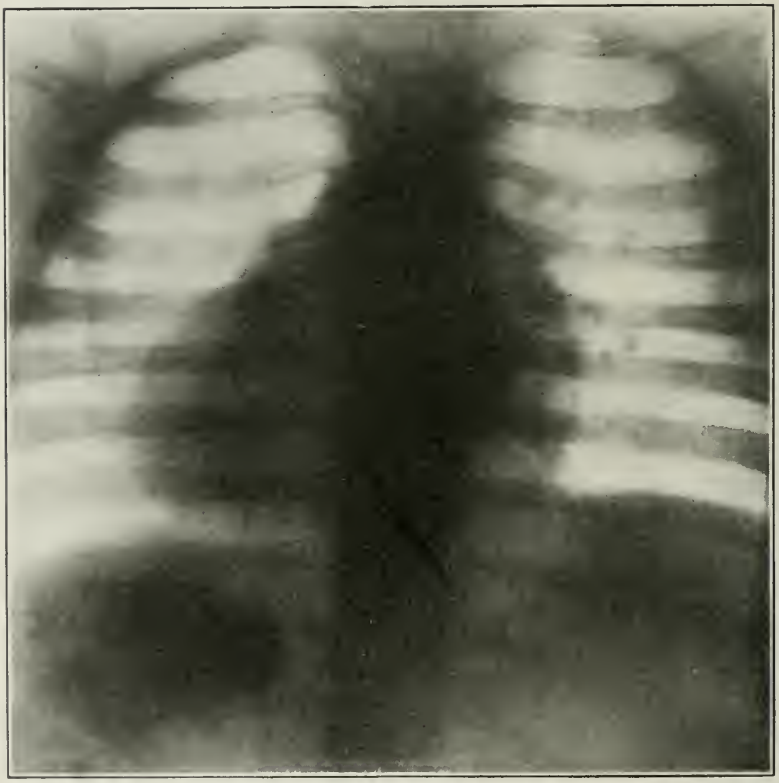

Fig. 10.—Same case. Roentgen picture taken after bismuth meal, following treatment by dilatation, showing that the bismuth has passed freely into the stomach.

Fig. 11.—Same case. On a recurrence of the symptoms, this radiograph was taken, showing the presence of a coin which was prevented by spasm from entering the stomach. It was removed with the aid of the esophagoscope.

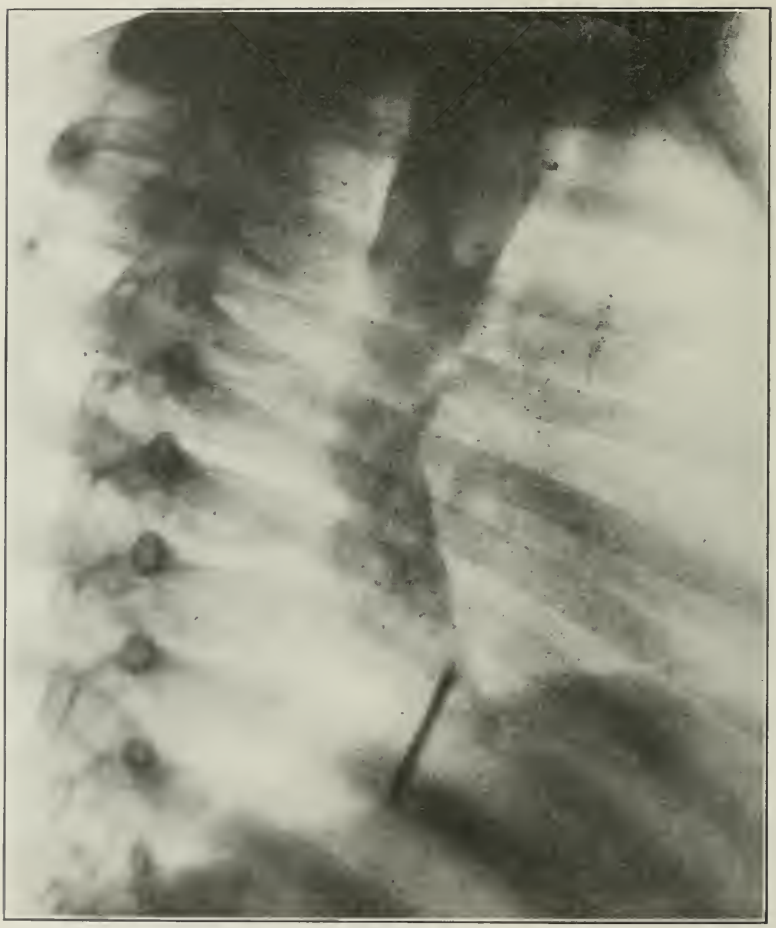

Fig. 12.—Same case. A week later, vomiting having recurred, the esophagoscope was passed and a piece of bristle discovered, which was removed. It had caused spasm.

of 25 cm. from the incisor teeth. The distance for a child of this age should be about 27 to 30 cm. The stricture was dilated and it was then found that a sound, 1.6 cm. in diameter could be passed. The child could then take soft solids without discomfort. Figure 5 shows the stricture after the obstacles had been removed. The child gained in weight and strength and after having the esophagus dilated at intervals, got entirely well, and on leaving the hospital was eating the regular house diet.

This patient is one who, from time to time, should be treated by dilatation through the esophagoscope, and will, under these conditions, probably continue to do well. The intervals for necessary dilatation will grow longer, and eventually dilatation will, in all probability, be unnecessary.

The history and appearance at the first examination inclined Dr. Greene to the belief that the case was one of organic congenital stricture of the esophagus at the cardia, but the subsequent ease with which the resistance gave way led him to believe that it was probably merely a case of cardiospasm. In the etiology of these cases of spasm of the cardia the congenital element is a likely factor. The spasm occurs at the point of normal constriction and is simply an exaggeration of normal spasm. This case, which represents a narrowing of the esophagus on the border line between a local organic condition and one of central spasmodic origin, is of a type exceedingly favorable for treatment.

CASE 3.—The third case is that of a boy 5¾ years old. He was normally developed at birth. So long as he was fed on liquids and soft solids he did not vomit. There was no history of anything corrosive having been swallowed. When he was 5½ years old he began to vomit everything that he ate.

Physical examination revealed nothing abnormal. The bowels had been constipated but he had complained of no pain and there were no other symptoms excepting the loss of weight. The urine was normal.

Bismuth meals were given and Roentgen pictures taken at intervals. These revealed nothing abnormal in the chest, and the bismuth had passed into the stomach and intestines, showing that there was no pyloric stenosis. Figures 6 and 7 show this. He was then given bread and milk and again vomited after taking a few mouthfuls. A stomach tube No. 34 French, was passed and met with a resistance at a distance of 24 cm. from the incisor teeth. The normal distance from the incisor teeth to the cardia at this age, according to Morse, is about 27 cm. After a short time the resistance gave way and the tube was passed into the stomach as shown in Figure 8. The tube was then removed, a bismuth meal given, and a Roentgen picture again taken. Figure 9, the child lying on his face, shows the esophagus entirely full of bismuth and the presence of a stricture near the cardiac end of the stomach. He was then treated by having the stricture dilated every four hours. Later a bismuth meal was given without the tube and a Roentgen again taken. This (Fig. 10) shows that the bismuth has passed freely through into the stomach. Some days later he began

to take liquids, having the tube passed only once a day for two weeks. After this he was able to take house diet without vomiting.

Dr. Greene at this time passed the esophagoscope and found that the esophagus was unusually roomy above the cardia, especially at its lower third. Spastic closure of the cardia was noted but this was relieved by slight pressure and the esophagoscope was passed through it. There were no signs of bagging of the esophagus nor any pouch, and the spastic closure of the cardia was always easily obliterated by slight pressure.

The child remained perfectly well for two weeks and then began to vomit everything, even water. A Roentgen picture then showed the presence of a foreign body in the esophagus, and Dr. Greene, by means of the esophagoscope, removed a quarter dollar. Figure 11 shows the quarter prevented by the spasm from entering the stomach. The child then seemed perfectly well and there was no vomiting for a week. He then began to vomit again and when the esophagoscope was passed it revealed a piece of bristle just above the cardia. This was easily removed by forceps. Figure 12 shows the bristle. Since this time the child has occasionally had a slight spasm of the esophagus and dilatation has been done once or twice. The spasm, however, is growing less and probably will soon cease to appear. The child did not seem to be of a nervous temperament and his parents were not neurotic.

There seem to be two classes of esophageal narrowing irrespective of those of traumatic origin. Both classes will probably be found to be of congenital origin. One of them, however, is a localized organic condition in the walls of the esophagus, while the other is a functional, with possibly an additional organic, congenital condition of a brain center, which is represented by a lack of inhibition.

It is possible that pure spasms of the esophagus are mostly congenital and are located in the brain.

197 Commonwealth Avenue.

DISCUSSION

DR. GRIFFITH: These cases of congenital malformation of the esophagus are very rare and very interesting. They are of different forms, the most frequent being obliteration of the esophagus with tracheo-esophageal fistula. Of Mackenzie's sixty-three cases of esophageal malformations, forty-three were of this nature. I had the pleasure of reporting, in conjunction with Dr. Lavenson, an instance of this variety in 1908. In connection with this case we made a critical review of the various other malformations which had been reported in medical literature. Unless there is a great advance in surgical knowledge there is practically nothing to be done for most esophageal malformations. In many the esophagus is obliterated throughout a large part of its extent, sometimes being reduced to a mere fibrous cord: and it would be necessary to reconstruct an almost entirely new esophagus. In most other forms of malformation in this region the surgeon encounters equally difficult or impossible problems.

NEEDLE IN THE HEART FIFTEEN MONTHS; DEATH; AUTOPSY

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CASE: *R. Z., aged 2 1/4 years, under observation at the Presbyterian Hospital, N. Y.; accident when 1 year old; died; autopsy.*

A puny, undersized child was brought to the out-patient department of the University and Bellevue Hospital Medical College, the parents hoping that she might be strengthened, her color improved, her bronchitis cured. She was announced to me among the material for clinic as "congenital heart disease." She was not cyanotic. I put my hand over her chest and felt the purring thrill. I presumed it to be a case of congenital heart in which there was no cyanosis, an exception to the rule. On further examination it was noticed that the murmur, though loud and purring, was heard all over the chest, and was not of maximum intensity over the left space and costo-sternal junction. The maximum was rather over the belly of the left ventricle. The physical signs were exceptional and not at all convincing; but since the child was so young and had no previous history of illness, it was presumed that it must be really a case of congenital malformation without cyanosis. The unclassical points here mentioned led me to make an effort to get the child into hospital for further observation. When it arrived at the Presbyterian Hospital I went through the same preamble to the staff. After two examinations I asked for a radiograph, to learn the size of the right ventricle and for any chance information that might be gained. The accompanying illustrations show what the *x*-ray revealed (Fig. 1). One plate exposure caught the heart just in contraction and gave two parallel shadows. Two right-angle exposures located the foreign body in the cavity of the left ventricle.

Amusing stories are told of the weird effect that the first developed plate had on the photographer. It is said that he believed the plate had a defect in it; that in the second plate the camera was defective; in the fourth and fifth and subsequent plates that his brain was touched. I cannot vouch for these stories.

Now that the diagnosis was made, the question arose, How was the needle to be removed? While the surgeons were discussing the matter the child developed bronchitis. She recovered from this, and after remaining in the hospital for a month or more, it was thought best to remove her to the country. There was no hope for the removal of the needle and really no hope of the child's living in her present condition. After a short sojourn in the country the child returned suddenly to the hospital with pneumonia, and died within twenty-four hours and consequently was a coroner's case.

The coroner made a most careful and thorough autopsy, and I am able to give a completed history. The needle was found as predicted, free in the left ventricle, butt-end down (Fig. 2). The needle was slightly corroded. There was no ante mortem clot and no inflammatory action about it. It pierced and extended beyond the mitral valve and scratched the endocardium of the auricle. In the auricle there was an area of superficial ulceration where the point of the needle had rubbed off the endothelium. The apex of the heart was adherent to the pericardium about the region through which the needle went, for an area the size of a quarter of a dollar. There was also a little roughening of the pericardium about the adherent area. This was the sum total of the irritation which the needle gave in its travel through the diaphragm and pericardium. On the under-side of the diaphragm was a streak of rust or dark staining (Fig. 3), showing the course by which the needle had traveled from the abdominal cavity to the ventricle.

The needle entered the abdominal cavity by way of the skin surface, presumably at the time of the fall at the age of 1 year. By one thrust it was shoved into the very apex of the heart, the butt-end of the needle remaining just within the skin of the abdominal wall, the point possibly extending even into the cavity of the ventricle. The point of entrance into the skin was at the most exactly near point, viz., at the left side of the ensiform cartilage close up to the ribs; likewise, the exact point of entrance into the apex was at the septum. The direction of the needle was such as to miss the right ventricle and proceed straight to its resting place in the left heart. There was no evidence that the needle had touched the liver or done injury to any other abdominal tissues or organs. After the first thrust, it is easy to know its mode of advance. Every muscular contraction sent it forward on its way, point foremost, till it lay free in the cavity of the heart. The butt-end was free in the cavity's

apex, and since the needle was longer than the cavity, the point extended up into the auricle, as mentioned above, thrust through the one leaf of the mitral valve.

There is but little authentic history, but this is a summary of what the parents gave. The child was, on entrance, 2 years old. When 1 year old, it fell out of a wooden cradle. At that time the mother noticed a

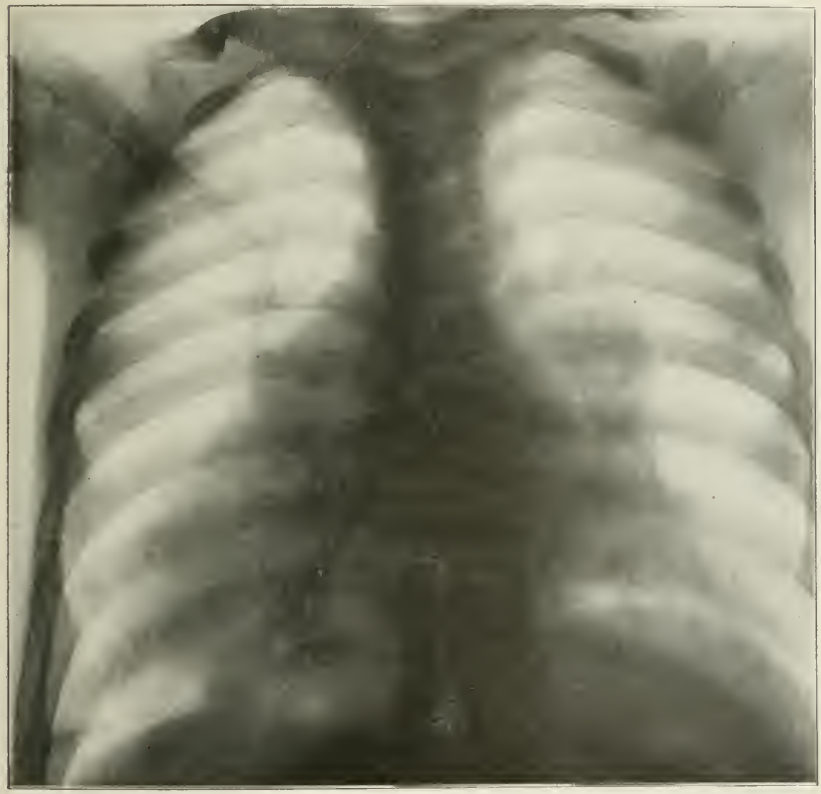

Fig. 1.—Needle fifteen months in the left ventricle of a child 2¼ years old.

protrusion just below the ensiform cartilage in the mid-line, "like a nail," "as if the child had swallowed something," but the mother knew nothing of anything swallowed. She said that she took her to a doctor who felt the swelling, but said it would go down, and so it did. There was no abrasion of the skin anywhere. The fall gave no severe results

at the time, though the mother says that since that time the child has gradually failed. In one conversation there are stray remarks that the swelling did not come till two weeks after the fall; that there was pain; that she took her child to the doctor for pain, and that there was stomach trouble. One cannot doubt that there may have been pain and gastric disturbance, but in that class of observers exact details are not forth-

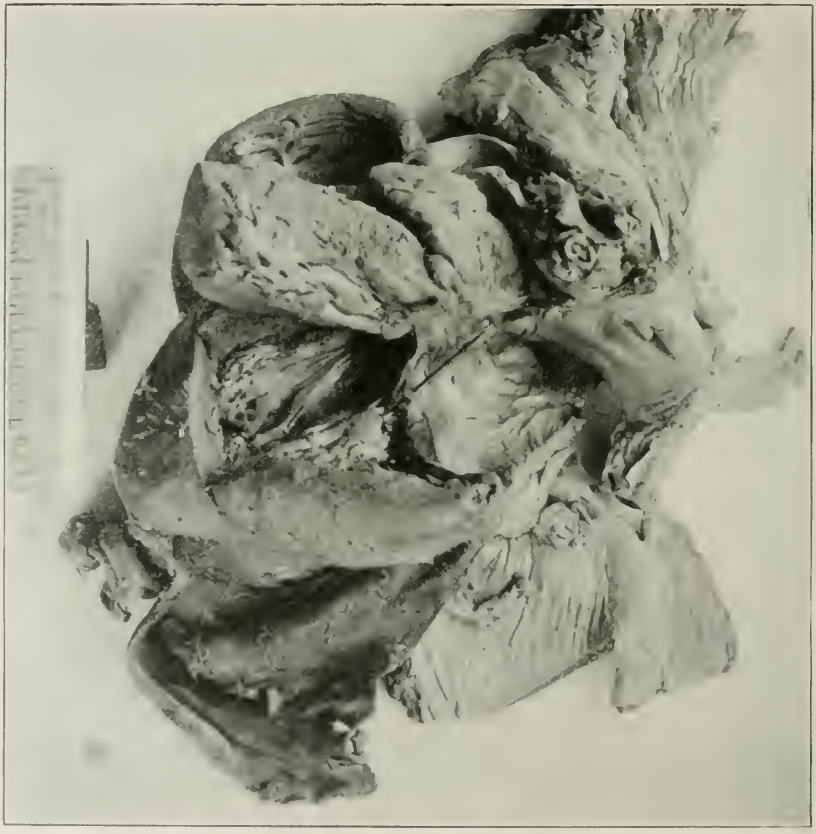

Fig. 2.—Needle in the left ventricle: point stuck through the mitral valve; butt-end is within the cavity of the ventricle.

coming. It may be believed that there was protrusion ("swelling") in the epigastrium; that there was "fever," considerable "heaviness of the chest"—dyspnœa, especially at night.

The hospital historian recapitulates as follows: Chief complaints, heaviness of the chest, at night; paleness; diagnosis, congenital heart lesion.

Twelve days after the child was sent to the country to build up its strength and blood, it returned with symptoms of pneumonia, and the same day it died. An autopsy was made. The photographs show the needle in position.

While this case was the absorbing topic of conversation, a patient waiting in the hall heard something said which stimulated the father to offer a remark of interest in this connection. "Why, my baby had a

Fig. 3.—Needle in the left ventricle. Dark line near the measure is the scar showing the track through the diaphragm.

needle in her belly," he volunteered. "The nursemaid had a needle and thread stuck in the shoulder of her dress. She was dandling the baby up and down on her shoulder," peering, no doubt, far out the window to see the nearest policeman on the beat. "All at once the needle was gone, the child failed to be quieted by the dandling on the shoulder, and when it came time to put the child to bed there was noticed to be hanging out of the belly a thread. On pulling at the thread, out came a little more

thread and finally a needle. This conversation was volunteered, was repeated verbatim by each of the parents separately, and not in each other's presence. We purposely made little of the incident, and when they were not in the sight and hearing of each other, we asked them about it as though it were not of the least importance, and the father and mother repeated the same story in the same words. Both had been present at the extraction of the needle and thread, and both told the same story.

However the needle in the case here reported started on its way, there is no mystery as to its method of progression. Like all needles in the tissues, it progressed point first, each step being in time with some muscular contraction.

How the needle came to be in position to pass by one clean thrust from the outside world quite out of sight within the integument, is of course entirely conjectural. A nurse has suggested that some people prefer to sew the garments on rather than use safety pins. In such a case it is quite within the range of possibility that a needle was left in the diaper ready to be thrust forward as the child fell over the crib.

It is of little value to discuss the physical signs of this unusual lesion. However, the murmurs were of nearly every variety. Over the belly of the ventricle the murmur was double; at the apex it was loud systolic; at the base it was also systolic and loud. The heart was large.

The condition of the needle was also of interest. One might suppose that the needle would be much corroded and that an ante mortem clot would be found. On the contrary, there was but little corrosion. As seen in the picture, there were little beads along the shaft, but not much. There was no sign of clotting before death.

The needle was the ordinary one used in sewing coarse garments, or, more properly, undergarments. It was about two inches long. It traveled by the shortest route possible from the outer world to the ventricle. It seemingly entered at the side of the ensiform cartilage, went straight to the apex and so on to its place in the ventricle.

It is useless to discuss the possibility of its removal during life, and yet it was a fascinating ground for speculation at the time. A powerful electro-magnet was suggested by more than one. There was no hope for the child without surgical interference, and the needle had been in place for more than a year. It was also quite true, as the mother said, that the child was remaining stationary or losing ground in spite of the best of care. In short, there was little or nothing to lose by operation, and

possibly something to gain. However, there was no operation, and in the light of the autopsy findings, it is fortunate that there was none. The parents, I might say, were quite willing to have anything done that the surgeons could recommend. In fact, they threatened to take the child out and possibly try elsewhere if something was not done, which, being interpreted, meant an operation.

The child was in the hospital three months, became quite content with her surroundings, and yet she had these peculiarities to the very end. She never spoke a word to any one of the staff for two months, did not smile in that time, yet was quiet, sat up in bed and after the first few examinations and visitations, never cried. She was a weird little thing, sitting in her crib looking straight forward into the eyes of all callers, as though she but faintly saw them.

57 East Seventy-Ninth Street.

THE FURTHER STUDY OF THE ANATOMY AND PHYSIOLOGY OF THE INFANT STOMACH BASED ON SERIAL ROENTGENOGRAMS

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Although the advances in roentgenology of the internal organs during the past few years have been truly remarkable, developing it into a highly specialized division of medical science, comparatively little research work has been done in the department of pediatrics. This was apparently not due to lack of inclination, but to the natural limitations imposed by a technic not sufficiently developed to make extended work with infants and young children possible.

The long exposures formerly necessary made it impractical to get radiographs of unruly infants with any detail, and, furthermore, there was always the danger of injury. Anesthesia was therefore often necessary when dealing with these young infants.

Flesh and Pietri in 1911 did pioneer work in this direction when they attempted to determine the normal stomach of nurslings and children, using bismuth or barium in their feedings. Their findings are mainly based on the results of fluoroscopic examination. Although this method is valuable as an accessory in such a study as ours, it had the great disadvantage of introducing the element of the personal equation, not allowing the findings to be checked up by other observers. As will be indicated below, their findings cannot be substantiated in the light of more modern methods.

The radiographic work was done in the Edward N. Gibbs X-Ray Laboratory (Carnegie Laboratory, New York University) by the director, Dr. L. T. LeWald.

TECHNIC

All the radiographs were made with the subjects in the vertical position. All were taken with the plate at a uniform distance of 24 inches from the anode. The exposures were all instantaneous and taken at the height of inspiration. Markers were placed on the ensiform and umbilicus. The tube was focused on the umbilicus.

Bismuth subcarbonate was mainly used, with the exception that bismuthoxychlorid was employed when an absolutely neutral salt was required. The proportion of bismuth used was approximately 10 gm. of bismuth to the 100 c.c. of feeding. The majority were fed by gavage unless a special experiment relating to the food itself was in progress.

It was natural for the early observers to compare their findings with recognized types of adult stomachs which had become, so to speak, standard—such as the Holzknecht type or the Rieder or "J"-shape or fish-hook type, which is the accepted type of adult stomach. The child's stomach approaches it more nearly after the second year. It was found, however, that the form of the stomach depended on the age of the child and the character of the food ingested, but on account of the imperfect apparatus they did not find that the x-ray gave them any help in studying the functionating ability of the stomach.

METHOD OF STUDY PURSUED

Our own study was planned for the purpose of determining if possible (1) the normal size and shape of the infant's stomach; (2) its relation to the neighboring organs; (3) the influence of the internal organs on the viscus; (4) its behavior under differing amounts of food; (5) influence of different types of food as liquid or solid, acid or alkaline; (6) its peristaltic action; (7) the motility; (8) the passage of food through the gastro-intestinal canal; (9) the application of this knowledge to certain pathological conditions.

The age of the infants studied varied from the new-born of 2 days to 20 months. Serial Roentgenograms made this study possible. The reproductions eliminated the personal equation and enabled us to reach certain conclusions.

At first infants were purposely selected at random; later those considered quite normal were studied, and finally those showing pathological conditions, as malnutrition, rickets, syphilis, pyloric obstruction, spasmophilies, tuberculosis, etc. The interval between the administration of the meal and the first exposure was from one to five minutes. Subsequent exposures were made at intervals of ten minutes to twenty-four hours in a given case, depending on the character of the experiment under way. We did not lose sight of the fact that this work was one-sided and that certain elements of error might occur, but we did hope that we could add something to the investigations previously made in physiological laboratories, eliminating the error of test-tube work and interfering as little as possible with the natural processes going on in the infant's stomach.

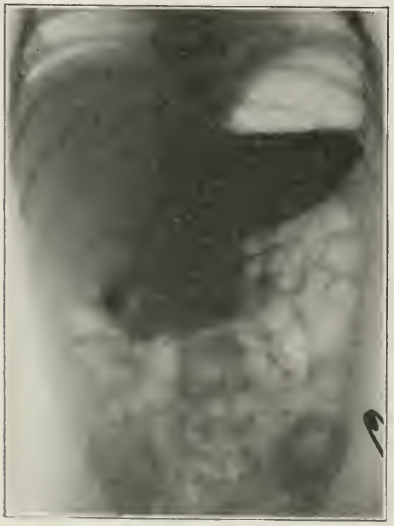
At this point it may be of interest to state that independently of our efforts and unknown to us, Alwens and Husler of Frankfort were engaged in a problem apparently along similar lines; wherein our findings differ from these observers will be indicated later.

Series A—Figure 1.

Series A—Figure 2.

Fig. 1.—Series A. Baby T., aged 2 days; nursling; 13 drachms fermented milk and bismuth introduced two hours and twenty-five minutes after last nursing. Exposure one minute after administration of food. Note size and shape of stomach and the gas area; a fairly large quantity of food has passed through in this time.

Fig. 2.—Series A. Same infant as in Fig. 1. Exposure after forty minutes. Note contraction of stomach and that large proportion of the food has entered the intestine.



Series B—Figure 3.

Series B—Figure 4

Fig. 3.—Series B. Aged 2 days; breast fed; 15 drachms given two hours and thirty minutes after last nursing. This exposure two minutes after the feeding. Note large size of this new-born stomach, about one-half gas and one-half food; a considerable amount of food has passed through pylorus in two minutes.

Fig. 4.—Series B. Same as Figure 3. Thirty-seven minutes after feeding; pyloric end still to right side of median line; food throughout jejunum.

Series C—Figure 5.

Series C—Figure 6.

Fig. 5.—Series C. Baby B., male; aged 4 days; nursing baby. Exposure after two minutes; 1¾ ounces food given two hours and forty minutes after last feeding. Note large size and peculiar shape of stomach; greater curvature at the umbilicus; food already extruded into jejunum.

Fig. 6.—Series C. Same infant as in Figure 5, thirty minutes after feeding; the greater part of the food has passed through into the small intestine; stomach has contracted only slightly. Remarkable decrease in amount in twenty-eight minutes.

Series D—Figure 7.

Series D—Figure 8.

Fig. 7.—Series D. Baby L., aged 4 days; nursling; 15 drachms bismuth mixture about three hours after last breast feeding. Exposure after two minutes. Note large gas area; pars pylorica is visible; some food already in jejunum.

Fig. 8.—Series D. Same infant as in Figure 7, twenty-three minutes after feeding. Note the transformation in shape to tobacco-pouch form. Stomach almost empty after twenty-three minutes. Food throughout small intestine. Note stream of food pouring out through pylorus.

Series E—Figure 9.

Series E—Figure 10.

Fig. 9.—Series E. Baby P., aged 11 days; nursling; two hours and twenty minutes after nursing 2½ ounces bismuth-milk mixture introduced. Exposure after five minutes. Note amount of food for age and stomach only one-half filled; large gas area; considerable portion of viscus passes to right of median line; greater curvature here well marked and reaches the umbilicus; only traces of food have gone through.

Fig. 10.—Series E. Same as Figure 9, forty-five minutes after feeding; a peristaltic wave is seen passing over the greater and lesser curvature; the antrum is drawn out spindle shaped; large deposits of bismuth appear low down in intestine.

Series F—Figure 11.

Series F—Figure 12.

Fig. 11.—Series F. Baby, aged 9 weeks; normal baby; breast fed; complemental feed just begun; 2 ounces bismuth mixture given. Exposure two minutes later. Scotch bag-pipe form; pylorus 4 cm. to right of median line; large amount of gas in cardiac end.

Fig. 12.—Series F. Same as Figure 11. Twenty-four minutes after feeding; remarkable decrease in amount of food in this interval; food is seen in jejunum.

Series G—Figure 13.

Series G—Figure 14.

Fig. 13.—Series G. Baby J. J., aged 2 months; weight, 7 pounds; always artificially fed; poorly developed; 45 c.c. bismuth mixture introduced. Exposure after five minutes. Illustrates tobacco-pouch or retort form (a form more apt to occur in weaklings); note amount of food in small intestine; stomach entirely to left of median line; bismuth pouring out.

Fig. 14.—Series G. Same as Figure 13 after forty minutes; shape has changed from retort form to pear shape; child nursed 22 drachms eagerly twenty minutes after gavage feeding; no admixture of the food has taken place; the gas area increased, probably through sucking action.

Series H—Figure 15.

Series H—Figure 16.

Fig. 15.—Series H. H. W., aged 4 months; artificially fed; malnutrition; 125 c.c. bismuth milk mixture; eight minutes later stomach pouch or retort form; pylorus in median line and relaxed; stream of food pouring out. Note amount of food that has escaped in this interval.

Fig. 16.—Series H. Same as Figure 15 after fifteen minutes; large amount of gas in cardiac pole; the heart pushed upward thereby.

Series I—Figure 17.

Series I—Figure 18.

Fig. 17.—Series I. A. S., aged 5½ months; weight, 9 pounds, 14 ounces. Diagnosis: Rickets with enlarged liver and spleen; pulmonary tuberculosis. Took 8 ounces bismuth milk mixture. Exposure five minutes later. Previously fed on a proprietary food; stomach much enlarged; extends well over to right of median line; the shadow of the liver and tuberculous deposits in the lung are well shown.

Fig. 18.—Series I. Same as Figure 17 after twenty-five minutes; stomach contracting on its contents. Note change in shape; possibly the precursor of the water-trap type of stomach; extruding large quantity of food.

Fig. 19.—Series I. Same as Figure 18 forty-five minutes later. Conformation entirely changed; only small amount of gas is left; food is seen passing out of pylorus in median line.

Series L—Figure 20.

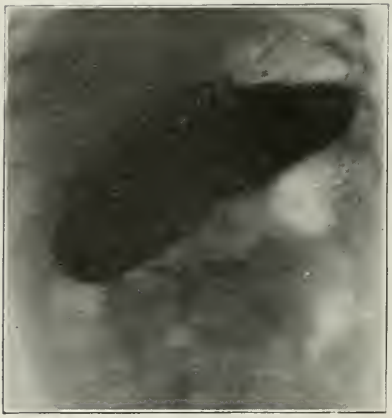
Fig. 20.—Series L. F. L., aged 7 weeks; weight 10 pounds; artificially fed practically from birth; 100 c.c. of bismuth-milk mixture. Exposure after five minutes. Note horizontal position and pyloric end under right lobe of liver.

Series L—Figure 21.

Series L—Figure 22.

Fig. 21.—Series L. Same as Figure 20 after twenty minutes; marked diminution in size; food being forced into intestine; baby now given 3 ounces of its usual formula twenty-five minutes after the feeding by gavage. Note subsequent exposure.

Fig. 22.—Series L. Same as Figure 20. Forty-five minutes after initial feeding the foods have not intermixed.



Series N—Figure 23.

Series N—Figure 24.

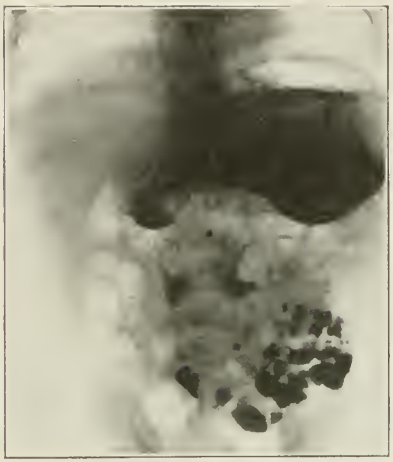
Fig. 23.—Series N. E. P., aged 3 months; weight, 10 pounds, 4 ounces; 100 c.c. top milk, (20 per cent.) + 2 drachms lime-water and bismuth oxychlorid (neutral) used. Example of delayed pyloric opening; one minute after feeding practically no food has passed.

Fig. 24.—Series N. Same as Figure 23 after twenty minutes; in comparison with other feedings an exceedingly small amount of food has passed through.

Series O—Figure 25.

Fig. 25.—Series O. G. M., aged 4 months. Diagnosis: Rickets; spasmophilic infant. Feeding: 6 ounces of 20 per cent. cream, ½ drachm of sodium bicarbonate with 10 per cent. bismuth. Exposure after five minutes. Note horizontal position and large gas area with enormous dilatation of cardiac pole; little food has passed.

Series O—Figure 26.



Series O—Figure 27.

Fig. 26.—Series O. Same as Figure 25 after fifteen minutes. Amount passed through in this interval decidedly small by comparison.

Fig. 27.—Series O. Same as Figure 25 after one hour. Change of form accompanied by the exit of some food after an interval of forty-five minutes. Since last exposure, alkalinity apparently has been overcome.

Series P—Figure 28.

Series P—Figure 29.

Fig. 28.—Series P. McC., nursing baby, 2 days old, well nourished; birth-weight, 7½ pounds. Exposure made two minutes after having food, consisting of 6 gm. bismuth in 60 c.c. of milk. This is considered to be one of the normal types of infant stomach.

Fig. 29.—Series P. Same as Figure 28 twenty-eight minutes after original food. Note the amount of food which has passed through the pylorus and how it is scatteered through the small intestine. This is considered a normal rate of emptying.

We approached this work with rather fixed ideas as to the natural conformation of the infant's stomach, but these were soon dispelled. Our ideas were those generally accepted, and it may not be amiss to quote from some standard text-books the description of this viscus, as it will emphasize the importance of checking up the present-day anatomical knowledge with Roentgenograms.

ANATOMY

Cotton, in his text-book on "Diseases in Infancy and Childhood," says of the stomach:

> Contrary to generally accepted statements the general form and position of the stomach are very similar to the empty and collapsed stomach of the adult, but in consequence of the large size of the left lobe of the liver, the whole anterior surface is usually covered by that organ. When the stomach is filled, the movement of its pylorus towards the right side is probably impeded by the large liver, thus tending to make the axis more vertical. The fundus is usually less pronounced and the valvular constriction of the cardiac orifice is wanting, allowing easy regurgitation of the contents. The average capacity at birth is less than an ounce.

In Holt's Diseases of Infancy and Childhood, the description reads thus:

> In the newly-born child it lies somewhat obliquely in the abdomen, and at the end of infancy has almost reached the transverse position. The stomach at birth is nearly cylindrical, but the fundus increases in size rapidly during the first year, although it does not reach its full development until quite late in childhood.

Chapin and Pisek in their book say:

> The stomach is somewhat like a vertical sac at birth, but gradually develops in a horizontal direction.

As a result of our investigations we are forced to the conclusion that there is no definite normal type of stomach in the infant. It is horizontal rather than vertical in position when compared with the adult type, and follows certain rather definite forms. We can distinguish (1) the ovoid, or Scotch bagpipe shape of Flesh and Pietri; (2) the tobacco pouch (or retort shape of Alwens and Husler), as previously described by us; (3) the pear-shaped stomach with base above and to the left. The shape of the stomach does not even depend directly on the amount or character of the food ingested, but rather on the quantity of gas which it contains or acquires. Furthermore, its limits are greater than we were accustomed to believe, extending to the liver on the right and at times filling the entire transverse space from one abdominal wall to the other.

The upper border or smaller curvature may or may not be seen in the Roentgenograms, while the lower border is formed of an indeterminate portion of the viscus.

Of particular interest from the standpoint of diagnosis is the position of the pylorus. In the majority of cases this is found comparatively high and behind the pyloric third; at times its position cannot be determined even though we clearly see that the food and bismuth has passed out of the viscus. This is especially true in the tobacco pouch form, in which the pylorus is forced posteriorly.

Alwens and Husler report that they have observed a change in form from the tobacco pouch to the bagpipe variety after the intestines have been emptied. This finding also occurred in our series (Figs. 13 and 14). The Rieder type was observed only once, occurring in a six-months old infant (Fig. 18). It appeared first as the bagpipe form, changed to a Rieder and then to a retort form. When semi-solid food is being taken comparatively little gas is swallowed and the stomach is more apt to simulate the adult or Rieder type. The question of contained gas, or introduced gas, is an interesting one. In some cases the gas seems to act as a buffer, preventing the over-distention of the stomach with food. As a rule, the broader or more protuberant the abdomen of the infant, the greater the amount of gas the stomach contains.

PYLORIC ACTION

One of our most noteworthy observations related to the rapid passage of food out of the pylorus—in a number of cases bismuth was seen in the duodenum one minute after the food had been introduced into the stomach by gavage, the average time being five minutes; in one case of the tobacco pouch, or retort form, the action was not unlike that of a siphon (Fig. 15); after the greater part had passed through the pylorus the emptying action became slower. Except in the instances in which semi-solid food (farina and bismuth) or cream were fed, the viscus tended to empty itself with unsuspected remarkable rapidity. How this action can be taken advantage of in cases of pyloric stenosis and pylorospasm has been indicated in a previous article.[1]

We must also question in this connection the advice of those who, like Grulee, recommend placing all infants on four-hour feeding intervals, since a large number of stomachs practically empty themselves within an

1. Arch. of Pediat., December, 1912.

hour. In abnormal cases, as in infants having chronic disturbances of nutrition the stomach began to empty itself very rapidly, and the emptying time was even shorter. If further proof is necessary as to the rapid emptying of the infant's stomach, it can be found in the fact that infants, to whom it was offered, greedily took their bottles of modified milk thirty to forty-five minutes after the feeding by gavage. This is well illustrated in Series G (Figs. 13 and 14), and also in Series L (Figs. 20, 21 and 22), Roentgenograms of an infant of 7 weeks who took 3 ounces of bottle feeding forty-five minutes after the administration of 3½ ounces of fermented milk and bismuth.

We attempted also to corroborate the suggestive experiments of Cowie and Lyon on the pyloric opening and closing reflex. It was impossible to record or obtain Roentgenograms of the action of the pylorus itself which they so well described, because as has been said above, the pylorus and the first part of the duodenum are rarely visible, but the retarding action, for example, of alkalies, which they record, is well shown in Series N (Figs. 23 and 24). Here the stomach did not empty itself for four and one-half hours. Again giving an infant, for example, one type of food, as fermented milk with bismuth, and then allowing it to take its bottle containing modified milk, we were able to verify the work of Cannon and the observations of Grutzer and Sick, who found that foods in the stomach do not tend to intermix. Sick goes even further and says that with fluid food we have the formation of true layers, so that in milk digestion we have the whey expelled first, later the casein and last the fat content.

STOMACH TONE

Observations on the contracting power or tone of the stomach can also be made by this method. The normal stomach tends to expel its gas accumulation soon after the entry of food; it tends to envelop or surround the food, to diminish in size generally, to shorten its axis by drawing upward and to the left partly under the shelter of the diaphragm. This action is not as marked in infants who retain the tobacco-pouch form; here we observe merely a diminution in the size of the viscus.

A peristaltic wave passing along the greater curvature is caught on the plate at times (Series N; Fig. 23). It is more apt to be seen in cases of habitual vomiting or in infants having pyloric stenosis or spasm. We have very seldom observed the wave along the lesser curvature, but this is not remarkable in view of the fact expressed above that the smaller curvature is seldom in sight.

In conclusion it may be said that the field of research in this direction has merely been opened. There are many observations, particularly dealing with the food in the intestines, which need close study, especially in their relation to disturbances of the bowel function so frequent in early life.

How much help we can obtain in our pediatric practice by a Roentgen examination of the alimentary canal in infants and children will be apparent by a study of the statements just made and the illustrations shown.

36 East Sixty-Second Street—338 East Twenty-Sixth Street.

DISCUSSION

Dr. Ladd: I want to congratulate Dr. Pisek on the excellence of his plates, and no one can appreciate more than I, who have worked on the subject, the difficulties in getting good plates from infants. In order to get them quickly we must use the intensifying screen—and I understand Dr. Pisek to say that one was used in this case. It is very difficult in using the screen not to overexpose or underexpose the plates, but this method promises a great deal in the way of getting information in regard to the gastric condition. I am impressed particularly with the difference in the appearance of the stomachs from the point of view which Dr. Pisek showed and then from my own. Dr. Pisek took his plates from a child in an upright position, while mine come from a child lying on the stomach. The shape of the child's stomach can be shown better in the upright position. For the purpose of studying the emptying time of the stomach I do not suppose it makes any difference about the position in which the child is, whether it be horizontal or perpendicular. One cannot help being impressed with the great rapidity with which the stomach empties itself of a large portion of its contents within an hour or one and a half hours. For the complete emptying of the stomach, however, it may require from four to four and a half and even five hours, if the child is not subjected to a new feeding. What Dr. Pisek's paper shows, and what I tried to show yesterday, was the great lack of peristalsis observed in the stomachs of infants and young children as compared with adults. Peristaltic waves are not so marked, the contraction of the stomach taking place *en masse*.

Dr. Chapin: I have recently made a study of two babies who were each given a barium meal and then a radiograph was taken every half hour during the day. I found that the barium reached the rectum in seven hours. I can confirm what Dr. Ladd says about the complete emptying of the stomach, for towards the last it was very slow in these cases. The ingested meal began to leave the stomach almost immediately but it was several hours before the stomach was completely empty.

In studying the bowels by clysma, it was found that the barium reached the cecum in a few minutes and in one case it even went through the ileocecal valve. I believe there is a future along the line of roentgenography, as it has opened up a great field for study of the intestinal tract, both with regard to its anatomy and its physiological functions.

Dr. Cowie: I should like to ask Dr. Pisek what position the patients were in when the radiographs were taken. It has been my practice to have the

patient lie down with the abdomen against the plate. In this way we get an entirely different picture from that which I have seen to-day. I have watched for the appearance of the duodenal cap but have failed to see it. The position has something to do with this. The duodenal cap is not seen so well or so regularly when the patient is in the vertical position. For this reason I believe the patient lying on his stomach is in the best position for diagnostic purposes.

DR. HEIMAN: I wish to call attention to the fact that the capacity of children's and infants' stomachs varies materially. In weighing the new-born baby before and after nursing we found their capacity varied from 30 grams to 180 grams, which would confirm the radiographic pictures Dr. Pisek has shown here to-day.

DR. BLACKADER: I would like to ask Dr. Pisek what inference he draws from the time in which the stomach is found empty, as regards intervals of feeding, and also the difference in the time of emptying the stomach when various modified foods, alkalies, etc., are given.

DR. TALBOT: I would like to ask what happens to the gas in the stomach when the baby takes the feeding? There seems to be a tremendous amount of gas in those stomachs and it must be accounted for. I would like to know whether these babies cried from handling when you were getting them ready for the exposures? I am told by our roentgenologist that it makes a great deal of difference in the emptying time of the stomach if a baby cries or coughs.

DR. PISEK: In reference to Dr. Talbot's question as to what happens to the gas when food is ingested—the gas has a tendency either to be expelled upward or is forced downward into the gut; the gut is often found distended with gas that has gone down ahead of the food mass, as the stomach contracted on the food. We have all seen mothers who have learned the trick of placing their babies over their shoulder after the baby showed signs of discomfort, thereby causing an expulsion of gas. In a few moments the child would take more food. The gas has considerable to do with the amount of food that the child will take and I think this is a condition that we have to contend with in cases of marasmus and malnutrition.

Answering the question of Dr. Cowie, as to the position of the patient, I will say that I think the vertical position gives better results. The children were kept in a horizontal position and as quiet as possible when fed, before the roentgenograms were taken. The children were as a rule fairly quiet. Occasionally we had a child who fussed and cried. I made no particular note as to the comparative effect on the children who were quiet and those who cried. I will be glad to follow that point up in the future.

As to Dr. Cowie's question regarding the use of a mineral substance, the mineral weight of the food is a very small factor, which can be disregarded. One can also use colloidal bismuth and get shadows in that way. Regarding the addition of alkalies, there is delay in the emptying time of the stomach when they are used. The capacity differs greatly in new-born infants as was well shown in the babies examined from a maternity hospital. As to the time required for emptying the stomach, I will say that I pointed out on the screen how rapidly the stomach tended to empty itself. We found the average time to be practically three hours although there is sometimes a slight deposit of bismuth left. I put a tube into the stomach and tried to withdraw this bismuth or food but found that I could get no return by siphonage. I then added a certain amount of fluid and measured my washings. In this way I

obtained a dram or a dram and a half, so that the inference is correct that three hours is practically the emptying time of a child's stomach and often less than that.

I want to say a word in regard to Dr. Ladd's series of pictures. They were extremely valuable and suggestive and I do not believe many realize the amount of work that series represents. One closing remark for future workers in this field. Unless you have a good technician good results cannot be obtained. He must be a master technician, preferably a physician, interested and appreciating what you are trying to accomplish. I was fortunate in having such a co-worker in Dr. LeWald.

THE DIAGNOSIS OF INTUSSUSCEPTION BY X-RAY

IRVING M. SNOW, M.D., AND MARSHALL CLINTON, M.D.
BUFFALO, N. Y.

The following case presents so many points of interest that it is herewith reported:

History.—The patient was the third child of healthy parents, born after a normal labor. She was nursed, but the mother suffered from sore nipples so much that she cried each time the child was put to the breast. When the child was 5 weeks old it vomited a clear bloody fluid and some hours afterward passed a black, tarry stool, but showed no other evidence of illness. It was supposed that the infant had swallowed blood from a fissured nipple, but the mother immediately withdrew some clean milk with a breast pump, and it is possible that the symptoms were due to a slight intussusception which was spontaneously released.

For the next few weeks the baby was fed from the breast, but the milk began to diminish and it was given supplementary feedings of cow's milk and a malted food.

November 6. The child was now 3 months old; it took the bottle well at 3 a. m., and afterward slept. At 6 a. m., it refused the breast and seemed quite ill. The child commenced to cry with pain, vomit and pass frequent stools of mucus and blood. The fifth vomiting attack showed regurgitation from the small intestine.

Examination.—At 8 a. m., a rectal examination was made with negative results. Directly after the withdrawal of the finger a quantity of fresh blood flowed from the anus. The abdomen was relaxed and on palpation a sausage-shaped tumor, moveable and insensitive, was felt in the left upper abdominal quadrant. The temperature was normal, the heart strong and regular. No medicine was given and feeding was stopped.

Diagnosis.—Dr. Edgar McGuire saw the infant in consultation at 10 a. m., and considering the positive symptoms present, colic, vomiting, bloody stools and a tumor in the upper abdomen, agreed with the writer (Snow) that the child was suffering from intussusception. As Dr. Marshall Clinton had been selected to operate, to relieve the child, a warm, normal salt solution was injected under pressure into the rectum.

Following this the child became easy and comfortable and slept. The vomiting stopped and the bloody mucous stools ceased, and when Dr. Clinton examined the patient at noon it was impossible to outline the abdominal tumor. This disappearance of the tumor is explained by the progressive shortening of the mesentery which pulled the mass of gut to the post-part of the abdomen.

Fig. 1.—Bismuth filling large intestine up to beginning of the intussusception; small amount of bismuth in dilated small intestine above constriction.

It was, nevertheless, decided that the intussusception was not reduced and suggestion was made that a radiograph be made with the colon filled with bismuth emulsion.

At 4 o'clock the child was taken to the office of Dr. Leonard Reu, where two pictures were taken, after injecting the colon with bismuth

and acacia mixture; an additional amount of bismuth was injected between the first and second exposures.

The patient did not suffer from this manipulation and was taken home apparently undisturbed.

The radiograph showed an unreduced intussusception in the right upper quadrant of the abdomen. A small amount of bismuth emulsion had been forced through the gut above the point of constriction.

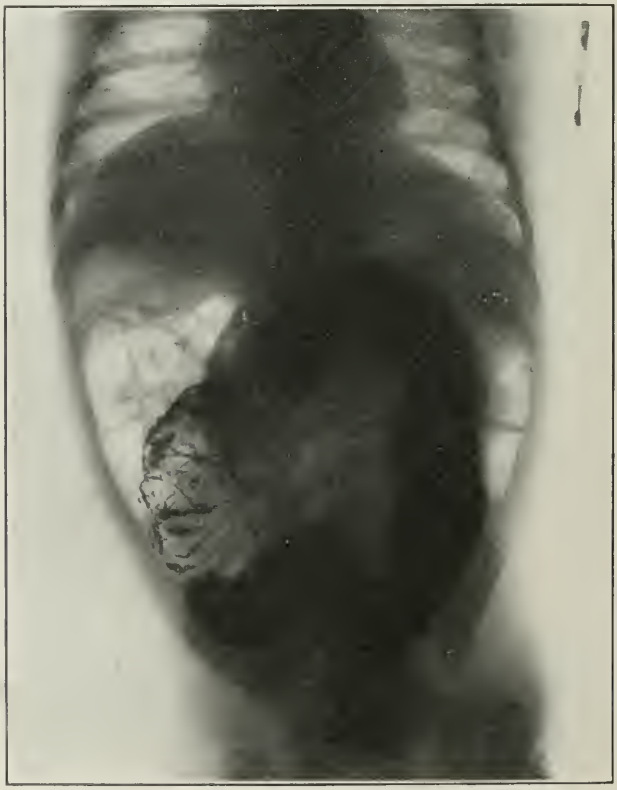


Fig. 2.—Bismuth forced under pressure alongside intussusception, filling large intestine up to ileocecal valve.

Late in the afternoon the temperature was 101 F., pulse 150, and the baby passed a bloody mucous stool.

At 7 p. m. the child was taken to the Buffalo General Hospital, where an operation was performed by Dr. Clinton.

Operation.—After iodin preparation of the abdomen and the administering of a minute hypodermic of morphin, under ether anesthesia, the abdomen was opened in the median line just above the umbilicus for 1½ inch. The abdominal wall was infiltrated with a 1 per cent. solution of novocain and then a 1 per cent. solution of quinin and urea hydrochlorid.

The intussusception was located by touch, and with two fingers the intussusception was squeezed out, with no attempt to bring it outside the

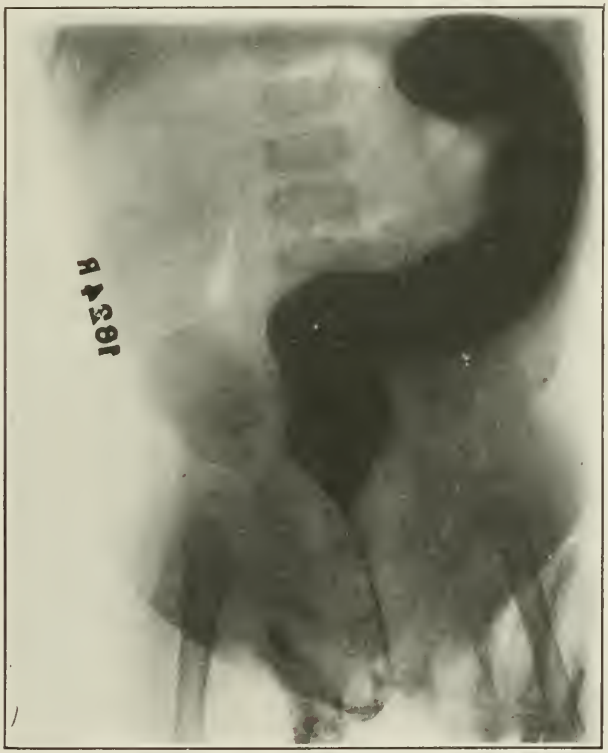


Fig. 3.—Dr. Parmenter's case of intussusception. Plate taken as soon after injection as possible, showing the obstruction at the splenic flexure.

wound. The invagination was ileocecal, ¾ inch of ileum being jammed into the cecum and colon.

After reduction, which was easily performed, the ileocecal junction was brought into the wound and three mattress sutures were placed in

the sides of the ileum and the wall to try to prevent a recurrence. A further infiltration of the peritoneum with urea solution was made before closing the wound, which was sewed up in layers in the usual way. Time of operation, twenty minutes. Time of operation after the onset of symptoms, thirteen hours.

Fig. 4.—Plate taken about three minutes after plate in Fig. 3, showing some of the bismuth forcing its way beyond the splenic flexure.

After-Course.—After the operation the child was taken home and 2 drops of paregoric and 2 teaspoonfuls of water were given per rectum every hour during the night.

Next morning the baby passed flatus freely and considerable bismuth mixture. Temperature, 100.4; heart rapid but strong. Child comfortable and had lost but one-half pound in weight.

There was a rapid convalescence, but as the mother's milk failed, and as cow's milk disagreed, it received and throve on condensed milk. At 7 months of age, 4 months later, the weight was 20 pounds.

The case was observed practically from the time the invagination occurred until operative relief thirteen hours later.

After giving a saline injection a deceptive amelioration occurred. All symptoms disappeared and the condition was masked for several hours until a radiograph was made.

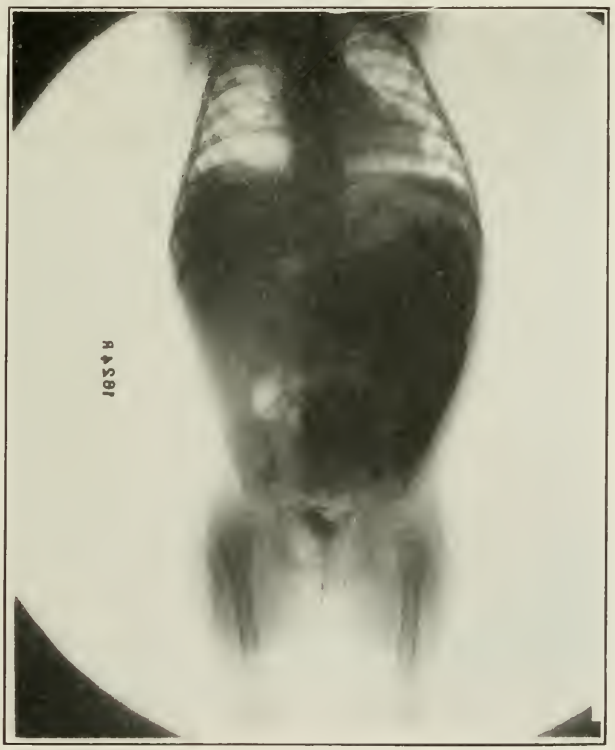


Fig. 5.—Plate made five minutes after plate in Fig. 4, and ten minutes after the injection, showing bismuth passing into the large intestine around the intussusception.

An additional case of intussusception diagnosed by x-ray is reported by Dr. J. Fred Parmenter as follows:

History.—G. B., aged 9 months, entered the Children's Hospital May 7, 1913, suffering from facial lupus vulgaris and malnutrition. Family and past history negative.

Present Illness.—June 17, 1913, after passing a good night and seeming in perfect health, the infant took food at 8 a. m. and had a large, yellow, normal stool at 9 a. m. At 10 a. m. the child suddenly vomited a large quantity of food and began to look quite ill. At noon, during rounds, a nurse called attention to the child, from whom she had just removed a bloody diaper. Abdominal examination showed a rather tender mass on the left side just below the umbilicus. Diagnosis of intussusception, and immediate operation advised, which was accepted by the parents.

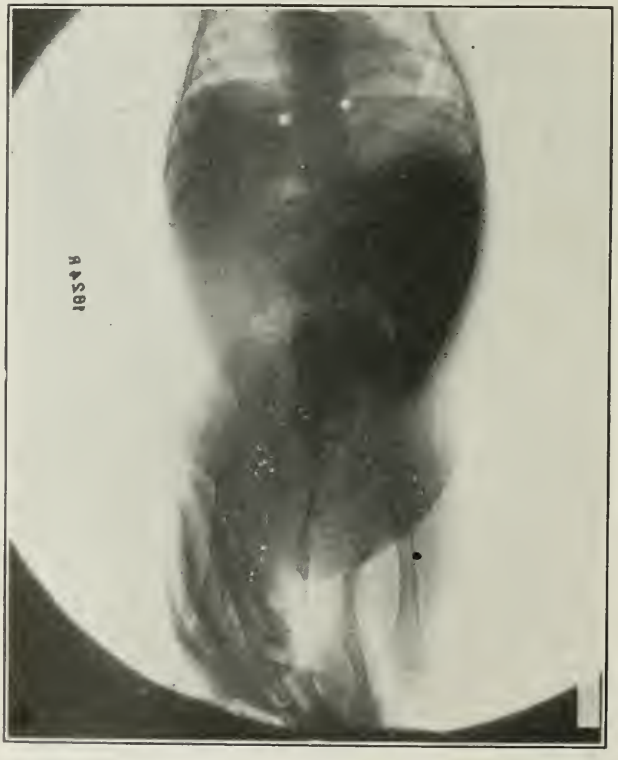


Fig. 6.—Plate made ten minutes after plate in Fig. 5 showing still more bismuth passing through.

Radiographic Diagnosis.—At Dr. Snow's suggestion radiographs of the colon were made at 1:30 p. m. by Dr. Leonard Reu, the bismuth solution being introduced per rectum, which verified the clinical diagnosis, as the accompanying plates will show, Dr. Reu's interpretation being as follows: Plate (Fig. 3) taken as soon after the injection as possible, one to two minutes, shows the obstruction at the splenic flexure. Plate (Fig. 4) taken about three minutes later shows some of the bismuth forcing its way beyond the splenic flexure. Plate (Fig. 5), five minutes after No. 2, and about ten minutes after the injec-

tion, shows more bismuth passing into the large bowel around the intussusception, while Plate (Fig. 6), taken ten minutes later, shows still more bismuth passing through. Patient's condition immediately improved after the injection, this being due to the slight temporary relief of the obstruction, which was producing shock. The patient vomited and had several bloody stools before the operation, which was performed by Dr. Parmenter, assisted by Dr. Joseph Lewis, at 3:30 p. m.

Operation.—Ether anesthesia. Iodin preparation, high median incision; intussusception found on left side, just below the splenic flexure, was delivered and reduced by gentle taxis and pressure on the colon side as suggested by Moynihan. The cecum and ascending colon were practically devoid of mesentery, which accounted for finding the tumor so early on the left side. It was deemed advisable to remove the appendix, which was done, and the abdomen was closed in the usual manner. The intussusception began at the ileocecal valve, and several inches of ileum were telescoped into the colon as far as the splenic flexure. Duration of operation eighteen minutes; uneventful recovery, to date, ten days.

The case is reported because of the opportunity afforded of making an early diagnosis and the unusual location. The intussusception was immediately diagnosed and operated on six hours after commencement of symptoms.

Inasmuch as the life of a patient with intussusception depends on an early diagnosis, and as the clinical picture may be atypical, with some important symptoms lacking, as abdominal tumor or intestinal hemorrhage, the aid of the x-ray in the diagnosis of suspected intussusception should come into common use.

As far as we are aware, ours is the first reported case in which a radiograph was taken to confirm the diagnosis of an intussusception.

476 Franklin Street.

DISCUSSION

DR. SOUTHWORTH: I think Dr. Snow has not stated how the bismuth was introduced. I should like to ask him how he introduced it?

DR. SNOW: It was given by two rectal injections of about 4 ounces of bismuth and mucilage of acacia.

WHY DOES THE OPERATION FOR REMOVAL OF ADENOIDS FREQUENTLY FAIL TO RELIEVE MOUTH-BREATHING?

H. M. McCLANAHAN, M.D.
OMAHA, NEB.

The lay public has been taught that mouth-breathing in children means the presence of adenoids, nothing more, and that certain relief will follow an operation for their ablation. This opinion prevails largely among members of the medical profession, and until beginning this study, that was my belief.

For many years I had noticed that the degrees of relief from mouth-breathing following adenoidectomy vary greatly in different cases. In some very slight and others prompt and decided. The following incident attracted my attention:

Aug. 1, 1909, I operated on a boy 8 years old for adenoids. There was slight, if any, relief from the mouth-breathing. Because the operation failed to give relief, the mother refused to pay the bill. While the mother's contention was correct, I was satisfied that the operation was thorough, that the vault of the pharynx was free from adenoids, and that the failure was not due to any fault of mine. To satisfy myself, and to determine, if possible, the reason for the failure, I began a study of the effect of this operation in children coming under my observation, not only patients on whom I had operated, but all who had received the operation. In the examination of children in my office, when I ascertained that a child had been operated on for adenoids, I made a study of the case, taking into account the following facts:

1. The facial expression.
2. The ability of the child to breathe through the nose with the mouth closed.
3. The appearance of the mouth and throat.
4. The condition and coaptation of the teeth.

In studying the facial expression I was careful to watch the child when it was unconscious of being observed, to note the general contour of the face, the outline of the nose, the size of the anterior nares, the relation of the lips to each other and the relation of the upper lip to the teeth, and its length.

Then the child would be requested to close the lips and breathe through the nose. First through both nostrils, then each nostril separately. It was the rule to find the breathing better through one or the other nostril, and also it was my observation that an obstruction in one nasal fossa induced mouth-breathing equally as well as when both fossae were obstructed.

In examining the mouth and throat, I would note the shape of the hard palate, its depth, and whether or not it was circular or angular in outline at the vault, then the condition of the throat and tonsils. The pharynx was examined by means of the mirror in all cases, and in twelve of the cases I explored the vault of the pharynx with the index-finger in order to ascertain by sense of touch the size of the posterior nares. In studying the position of the teeth I was careful to have the child close the teeth and then by separating the lips to note the relation of the upper to the lower teeth. It was this phase of the examination that gave me the most information. In the normal mouth the lower teeth are half the width of the bicuspid in advance of the upper, and the upper incisors overlap the lower, and cusps of all the teeth (except the incisors) are in apposition and proper alignment. In this condition the nasal fossae are normal in size, in so far as bony structure is concerned, with room for the free flow of air into the vault of the pharynx, unless some growth or inflammatory condition be present.

In this manner I have examined fifty-two children who had been operated on for the removal of adenoids. I am not able to give in all cases the date of the operation. These children ranged in age from 6 to 12 years. I purposely excluded all cases under the age of 6 years. Twenty-eight were girls and twenty-four boys. There were more girls than boys, for the reason that many of the girls were operated on for the cosmetic effect. Including my own cases, the operation had been performed by eight physicians; four of these are personally known by me to be competent operators, men whose practice is limited to the nose and throat. I emphasize this point because the failure to relieve mouth-breathing is often attributed to the lack of skill on the part of the operator. Almost without exception, I found that the mother was disposed to criticize the operator in all the cases in which the result was not satisfactory.

In twenty-eight cases the relief from the mouth-breathing was either complete or the condition was greatly improved. This was the verdict

of the mother and also my belief from the study of the cases. Of these cases there were six of whom it could be said there was more or less of the adenoid tissue in the vault of the pharynx at the time of the examination, yet the nasal breathing was quite free. But most interesting is the fact that in these twenty-eight cases there was fairly normal coaptation of the teeth. In one there was coaptation of the incisors without overlapping, but this child (a boy of 8 years) was not a mouth-breather, but in all, upper and lower teeth coaptated.

In twenty-four of the cases the operation was a failure in so far as nasal inspiration was concerned. Three of these cases had been subjected to two operations and one had been operated on three times, in each case by a different surgeon. In twenty of these twenty-four cases I am satisfied that the failure to relieve mouth-breathing was not due to faulty technic on the part of the operator or to recurrence of the adenoids, but to anatomic conditions in the superior maxilla. In the other four there were adenoids in the vault of the pharynx at the time of my examination, due either to recurrence or faulty technic. In these cases mouth-breathing was due to obstruction in the pharynx and not to defective development. In six of the twenty-four cases there was decided hypertrophy of the tonsils, but I do not believe these caused the mouth-breathing; however, I may say in passing that the history was that all of these children snored during sleep. In all of the twenty-four cases there was bad coaptation of the teeth, as well as distinct evidence of the maldevelopment of the superior maxilla, and the other bones in intimate relation to it, namely, the vomer, palatine and turbinal bone. The type of malformation in twenty of the twenty-four cases was as follows: The hard palate was deep and either circular or angular. There was retraction of the mandible due to its being drawn downward and backward and consequent apparent lengthening and actual narrowing of the superior maxilla, and in all of this number the upper lip appeared short and could be brought in coaptation with the lower lip by a strong muscular effort. This is the typical so-called adenoid face, but the appearance is due to defective development of the upper jaw.

Whether this maldevelopment is primarily due to adenoids in infancy occluding the vault of the pharynx, necessarily compelling mouth-breathing, or is a congenital defect, or due to other causes, is not the question. This phase of the subject was so well presented in the series of articles in the *Archives of Pediatrics* for January and February, 1913,

that I purposely eliminated from this paper a discussion of the etiology of the deformity.

The clinical fact is that some children will receive prompt and decided benefit from the removal of adenoids, whereas others will not. When there is an obstruction in the nasal fossae the result of the high arched palate narrowing its lumen or deflection of the nasal septum or thickening of the turbinates or neoplasms, one or all of these conditions lessen the capacity of the nose as a breathing organ. In these cases but slight relief will follow the removal of adenoids because the obstruction is in front of the vault of the pharynx. The clinical evidence of this anatomic condition is the appearance of the hard palate and the imperfect coaptation of the teeth. Indeed, with bad coaptation of the teeth, there is necessarily a deformity of the superior maxilla.

As a result of this brief study I am entirely convinced that it is possible to determine in advance whether or not relief from mouth-breathing will result from the operation of adenoidectomy. In a number of recent patients on whom I operated, and patients operated on by other physicians, whom I had examined, I have been able to say in advance whether or not the operation would give relief to the mouth-breathing, and this opinion has been verified by an examination of the case after the operation. I do not wish to be understood as saying that children with defective coaptation of the teeth should be deprived of an operation if adenoids are present. There are other valid reasons for their removal aside from mouth-breathing, but in this class of cases the operation should be the preliminary step in the treatment, and in justice to these children the parents should be informed as to the nature of the deformity and of the probability of relief by proper treatment. Five of the patients included in the above list have been under treatment for the correction of the deformity. In three of them the benefit from treatment has been very decided. Two are now under treatment. I have here a plaster cast of one of these cases. The second was made just one year after the first and illustrates very clearly the decided improvement. My conclusions from the study of these cases are as follows:

CONCLUSIONS

1. A careful examination of the patient before operation will determine with reasonable certainty the degree of relief that will follow the removal of adenoids.

2. When there is a deformity in the superior maxilla, a frank statement of the facts will relieve the operator from unjust criticism.

3. Where atomic defects exist parents should be apprised of the facts and given the opportunity to have corrective treatment instituted by the orthodontist.

4. The best evidence of such defect is malcoaptation of the teeth.

DISCUSSION

Dr. Heiman: I should like to mention the fact that I have had these cases and I think we have all encountered cases of a similar nature. It is a good plan to send them for orthodontic treatment; it usually requires from one to two years to correct the condition. We should all encourage the parents to send these children to the dentist. The point is well taken to inform the parents of the importance of these defects.

Dr. Chapin: I have noticed frequently the high gothic arch in cases of adenoids. Many children are operated on for adenoids that do not need an operation, but where there is a very high gothic arch I think it is a good thing. I agree with Dr. McClanahan that orthodontic treatment should be instituted and supervised by the physician. The dentist should carry out the orders of the physician.

Dr. Carr: The subject is of recognized importance. If the child is seen first by a dentist who finds that the teeth are irregular, he ascribes all defects in nutrition to the dental irregularities. If a laryngologist is first consulted, he may find obstruction from adenoids and tonsils impairing the child's breathing capacity. A rhinologist sees a deviated septum and hypertrophied turbinates. Some of these children have more than one defect. With growth and development at puberty there is a widening of the sphenoid bone which is the keystone of the arch of the base of the skull, the sinuses are increased in size and the face broadened. Some of the defects that are present in early childhood are—in a degree, at least—overcome during this growth. In a child with a high gothic arch, removal of adenoids and tonsils may be necessary, but in such cases there is not always immediate relief, and the teeth may require attention also to secure the best results. Neither the dentist nor the laryngologist, however, can claim all the credit for the correction of such a case. Each should work under the supervision of the pediatrician, who should judge of the amount of special treatment required and its effect on the child's physical and mental condition. In my experience, I have seen children made extremely nervous by dental appliances.

Dr. Holt: One cause for the continuance of mouth breathing after operation for adenoids is the narrowing of the bony pharynx by anterior projection of the vertebral bodies. Such a deformity I have observed in many defective children, also in others. In the former class it is always well to make an examination of the posterior pharynx; one is often amazed to find how small the space is between the vertebral bodies and the hard palate.

Dr. McClanahan: This paper was written because physicians are frequently criticised by parents or friends when the operation for adenoids fails to relieve mouth breathing. I wish to emphasize that a child after six years of age having this operation, if there be defect in the superior maxilla, will not receive benefit from the operation, but if parents are told that there are other abnormal conditions present beside adenoids and that it is probable that the operation will not relieve mouth breathing, this course will frequently save the physician from censure. However, if adenoids are present they should be removed even if there are other anatomic defects in the upper jaw.

REPORT OF A CASE OF RABIES

ALFRED HAND, Jr., M.D.
PHILADELPHIA

When it falls to the lot of one observer to meet in three years with two instances of an infectious disease so rare that there is, or was, doubt in the minds of some as to its existence in human beings, the other case reported elsewhere[1] being the first in which the diagnosis was accepted by the coroner's office in Philadelphia County, it is but natural for that observer to feel that the disease is on the increase. In view of the mortality, almost 100 per cent., but one recovery of a doubtful case having been reported, it would seem equally clear that rigid preventive measures should be instituted.

J. R. P., 9 years old, made his first visit to the receiving ward of the Children's Hospital of the Mary J. Drexel Home on Dec. 18, 1912, when he was brought in by the police patrol, shortly after he had been severely bitten in the face by a dog. The Resident Physician, Dr. Shoudy, to whom I am indebted for some of the notes made subsequently, described the lacerations as being, one at the right angle of the mouth, another through the right ala of the nose, a third at the right angle of the nose and a fourth in the middle of the forehead. Bleeding had been profuse. Pure carbolic acid, followed by alcohol, was applied, a loose stitch taken at the angle of the mouth and the wounds were covered with gauze wet with 1 to 1,000 mercuric chlorid solution. He was then taken home by the patrol with instructions to return on the following day. At that time the wounds were highly inflamed, considering the time that had elapsed, with far more reaction than Dr. Shoudy had ever observed to follow a dog-bite. The boy, when questioned, stated that his jaws hurt him and that it had been difficult during the night to swallow. His mother was then informed of the danger of hydrophobia and was urged to leave him in the hospital for the Pasteur treatment. As she refused to do this the hospital declined to have further responsibility of the treatment. His mother then stated that she would see the family physician and be guided by him, but when Dr. Shoudy telephoned him three days later, the boy had not been taken to him.

The next that was seen of the patient was on January 15, when he was brought by his father for treatment of an abrasion of the scalp from a fall while playing in the street. The Pasteur treatment was again urged but the intoxicated parent could not see the necessity of it "for such a strong boy."

On January 29, the boy complained of not feeling well and was drowsy. The next morning he had headache and pain in the throat; at 10 a. m. he was suddenly seized with what the mother said was a convulsion, but he did

1. Hand, White and Reichel: Report of a Case of Hydrophobia. Jour. Am. Med. Assn., March 29, 1913, p. 990.

not lose consciousness, for during it he told her that he felt that he would die. His mother also said that his face became very red and he went "mad." A physician was called and with the father took the boy in his carriage to the hospital at 3 p. m., the boy walking into the receiving ward. On being informed over the telephone of his arrival, I directed that he be given morphin ¼ grain, hypodermatically, and be placed in a small room by himself, with his finger-nails covered so that none of the attendants might be accidentally scratched; basins with bichlorid solution were placed in the room so that all who handled him could disinfect their hands at once.

On my first visit to him at 4 p. m. he presented a never-to-be-forgotten picture as he tossed around in the bed, lying down, sitting up, jumping from side to side, never still for a second, his face flushed a bright red and the pupils of his eyes widely dilated, giving to his face the characteristic hunted expression of rabies. There was an evident spasm of the pharynx for the saliva, which flowed profusely, could not be swallowed but was spat out at intervals of a few seconds with a gagging sound which could only, by the wildest flight of imagination, be said to resemble the barking of a dog. The saliva consisted of small sticky pellets floating in a watery secretion which filled a pus-basin in a few minutes. As the morphin had had no effect it was repeated, and with the hope of relaxing the pharyngeal spasm or at least of relieving its painful feature, of which the boy complained bitterly, a cocain solution was sprayed into the nasopharynx. The effect of this was immediate in causing the gagging sound to cease, and the boy, becoming less restless, sat up and said, "Oh, give me a drink of water." A medicine-glass, full was handed to him and he reached eagerly for it showing that the name hydrophobia is sometimes a misnomer (a possible explanation being that children are slower to appreciate that attempts at swallowing increase the painful pharyngeal spasm and so do not dread the attempt, or even the suggestion of swallowing caused by the sight of a glass of water as adults affected by the disease are said to do); he took a mouthful, closed his lips for a few seconds in a vain attempt to swallow and then expelled it forcibly with a cry which had a note of regret in it. His temperature at this time was 106 F. Immediately after his admission an attempt to give him a sponge bath was unsuccessful because of the intense excitement it produced, apparently mental as well as physical, for he talked rapidly and disconnectedly, with frequent expressions of fear that he would be hurt.

Physical examination was almost impossible owing to the fact that when he would become quiet momentarily, a touch would be enough to start up the wild restlessness again, but it was finally determined that the lungs were clear and that the heart-sounds were valvular, the pulse-rate being 200 per minute.

At my next visit, two hours later, in company with Drs. Griffith and Gittings, he was able to tell his name when asked, and in reply to the question if he had pain, he would put his hand to his throat and clench his fingers. By this time it had become necessary to restrain him by a sheet across the chest, but this only limited the muscular activity which kept up for another hour, periods of quiet becoming longer and a touch not interrupting them so easily. Dr. Griffith spoke of a certain resemblance in the high fever and muscular restlessness to grave chorea, but noted the difference in the mental states and in the presence of frothing at the mouth, the boy having ceased his acts of spitting and the saliva flowing out of the corners of the mouth. At 7:30 p. m. Dr. Shoudy noted free perspiration, pupils responsive to light and less widely dilated; breathing hard with increased tactile fremitus on the left; heart-action slower; not so easily excited but a sudden tap caused a general muscular con-

traction; convulsive movements still occurred with arching of the back and stiffening of the neck; did not reply to questions. At 8 o'clock the parents called and took the boy home where he died fifteen minutes after his arrival.

Upon the invitation of the Coroner's physician, Dr. Wadsworth, I accompanied him to the home on the following day but parental objections to an autopsy could not be overcome for three days. The material finally obtained was taken to the Laboratory of the State Livestock Sanitary Board where it was examined by the Director, Dr. Karl F. Meyer. His reports are as follows:

Feb. 5, 1913. Report on Specimen No. 3273, received February 3, consisting of the brain of a boy: A microscopical examination of sections of nerve tissue showed one ganglion cell containing three Negri bodies. Animals have been inoculated with an emulsion of this material.

Feb. 27, 1913. Final report on Specimen No. 3273, brain of J. P.: One of the rabbits inoculated subdurally died subsequently and microscopical examination of sections of the hippocampus revealed Negri bodies in large numbers. The diagnosis of rabies can be made conclusively.

DISCUSSION

DR. NICOLL: A year ago Dr. Poor, who has been in charge of the Pasteur treatment of the Department of Health for many years, asked me to see a boy who had been bitten on the hand three weeks previously and had come to the clinic for treatment. On examination the boy did not seem to have anything particular the matter with him. All he complained of was pain in the upper arm. I asked Dr. Poor if he had tested him with water. He said no. I then asked if I might do so and he said, "Don't, or he will get frightened and run away." Finally I asked the boy if he would not take a drink of water to clean his tongue as I wished to see if it was coated. He did so and gave a cry of pain and grasped his throat. I asked him if he had had the same pain previously. He said he had, as he sat in the elevated train by an open window when the draught struck his face. He died within two days. Dr. Poor told me that he had been absolutely certain of the presence of rabies in this patient from the expression in his eyes, which to him had the same hunted look as that seen in rabid animals.

PRESIDENT MORSE: It gives me much pleasure to introduce to the Society Dr. Harvey Wiley of Washington.

DR. WILEY (Guest): I came to learn and not to instruct. I have been very much entertained by these papers and also much informed. I am interested in this subject from a practical point of view. I have enjoyed very much being here and am only sorry I could not attend all of the meetings.

PAROTITIS COMPLICATED WITH MENINGITIS

GEORGE N. ACKER, M.D.
WASHINGTON, D. C.

The appearance of nervous troubles in the course of parotitis did not escape the attention of the older observers. Hamilton in 1758 recorded a case of death in a man of 22 years from meningitis complicating mumps; Astley Cooper the case of an infant who died after an illness of eight days; French in 1812, Malsbrouche in 1867 and Niemeyer have described these conditions without detail. Trousseau relates cases of men 17 and 35 years of age with severe meningitis which disappeared when orchitis supervened.

Gailhard in 1877 compared the meningitis and cerebral complications of mumps to rheumatism of the brain. He reported six cases with stupor, feebleness, slowness of pulse, rigidity of neck, headaches, hyperesthesia, photophobia, delirium and coma. In 1885 Lannois and Lemoine published an important memoir on this subject. They reported a case in which the meningeal complication of mumps was followed by aphasia and right hemiplegia, and was not well for some months. They considered these conditions to be dependent on meningeal lesions of the congestive and inflammatory order accompanied sometimes by lesions of the brain.

Dupre in 1884 proposed the term meningism for these cases, holding there was not a true anatomical alteration of the brain. In some epidemics parotitis appears to lose its benign qualities and causes grave symptoms. Writers have observed meningitis often in cases which have orchitis and are led to believe that such cases are more severe, yet in children, in whom orchitis rarely occurs, meningitis has been noted in a number of cases. The infant has a nervous system easily impressed, which has a tendency to respond to irritating morbid agents by an intense reaction, such as convulsions. This is increased by heredity, neuropathy and alcoholism. Acute meningitis is usually described under three periods: invasion, excitement and depression; each of these periods is marked by a series of symptoms which taken together make a clinical picture, as a rule, constant and characteristic. Such a description cannot be made in the meningitis of mumps. It is true that it may present all the symptoms of acute meningitis, but usually the symptoms take a

variable course; nervous complications are tolerably frequent, due to the involvement of both the central and the peripheral nerves. A meningeal reaction may present itself in connection with an attack of mumps, coming on two or three days after the swelling of the parotids, although in some cases it supervenes rather later. On the other hand, it has been known to precede the parotid enlargement by some hours.

SYMPTOMS

The meningitis in question manifests itself by a rise in temperature, headache, insomnia and general discomfort. As a rule, the pulse does not increase in rapidity in proportion to the rise in temperature. In exceptional cases the symptoms are much more severe, there is a sharp rise of temperature, with nausea, vomiting and constipation, there is some rigidity of the neck, Kernig's sign, pupillary changes, strabismus, showing an irregularity of the pulse, disturbance of sensation, and even paralysis of the cranial nerves. These are obviously symptoms of basic meningitis, which is the usual form in this connection. In some instances there are signs of cerebral irritation, delirium, convulsions, spasmodic contraction of the facial muscles, the tongue and limbs, monoplegia and hemiplegia, deviation of the eyes, aphasia, and among spinal symptoms, cutaneous hyperesthesia and pain in the back and limbs. Lesions of the nerves are sometimes consequent to meningitis or occur independently of it. In these cases the virus of mumps seems to attack the sheaths of the peripheral nerves, as well as the walls of the nerve centers.

Many attempts have been made to explain the nervous complication of mumps. Eichhorst attributed them to hyperemia of the brain due to compression of the internal jugular by the enlarged parotid; Jussoud and Groucher by the embolic bodies from the endocarditis due to the parotitis infection; Micilsky to meningitis; Lannois and Lemoine to a meningoencephalitis or perhaps a thrombosis of the sylvian artery. Comby attributed them more to an hysteria than parotitis; Gallavardin interpreted them as proving a true meningitis due to the poison of parotitis. According to Schottmüller, a post-parotitic meningitis should be regarded as a serous meningitis, with more or less of an accompanying encephalitis.

For a long time the meningeal symptoms which have appeared in mumps had been described, but their pathological character was disputed, and the terms pseudomeningitis parotitis and meningism parotitis employed to designate them. It was not until lumbar puncture was resorted to that a clear idea was obtained of the nature of these menin-

geal reactions. This showed that it was not a simple functional trouble, but an anatomical modification of the meninges. When in 1902 A. Monad practiced systematically lumbar puncture in the infants attacked by parotitis, and proved six times in eight a lymphocytosis of the cerebrospinal fluid as abundant as that which exists in tuberculous meningitis, he demonstrated that this disease is capable of determining an appreciable change in the meninges. The same has been confirmed by Sicard in infants, Chauffard and Boideu in 1904, Dopter, Netter, Comby, Hutinel, Nobècourt and Brelt and Feliciano in 1907. All found a lymphocytosis in parotitis that had many nervous symptoms. The fluid was clear, with numerous lymphocytes, as in tuberculous meningitis. There was a small amount of albumin, but no fibrin. In the latter disease the meninges are permeable to iodin, but not the first. Dopter states that in simple mumps the cerebrospinal fluid is normal in cellular elements. The lumbar puncture is useful, not only for diagnosis, but also for treatment, as the severe symptoms yield soon after its employment, as has been demonstrated by Chauffard and Widal. The lymphocytosis only lasts for a short time.

BACTERIOLOGY

That a diplococcus is the pathogenic agent which is the cause of parotitis there can be little doubt from the researches and experiments that have been made. In 1893 Laveran and Catrin described a characteristic diplococcus which they had obtained from the parotid, from the edematous tissue of the face, from joint transudates and from the blood in cases of this disease. In 1896 McCray and Walsh examined the saliva from Steno's duct in ten cases. They found a diplococcus six times. Bein and Michaelis in 1897 and Pick in 1902 reported a similar finding. In 1906 Feissier and Esmein examined the blood in forty-five cases and obtained a diplococcus in thirty-seven. These experiments have been confirmed in this country by Isabella C. Herb of Chicago, who isolated a diplococcus similar to that of the other observers. According to Dopter, the bacteriological examination of the cerebrospinal fluid and meningeal exudate collected after death was sterile.

In the autopsy made by Maximowitch in 1880 the surface of the brain was found edematous and congested with serofibrinous exudate adherent to the pia-mater; the pons and cord were hyperemic.

In 1,705 cases of parotitis observed, there were 158 cases of meningitis, but this does not give the true proportions, as many cases pass unnoticed by careless observers.

DIAGNOSIS

The quick onset would differentiate this from tuberculous meningitis, as the latter comes on slowly and does not tend to disappear; from cerebrospinal meningitis by the clear fluid and absence of the meningococcus. In some cases the parotitis is so slight as not to be noticed, and this adds to the difficulty of the diagnosis.

This meningitis generally disappears rapidly. The motor paralysis can last a long time, but finally gets well. The deafness and optic atrophy appear to persist. This usually harmless disease may develop very alarming symptoms and be followed by permanent damage to important organs, and even end fatally. Among the sequelae of the disease Joffroy mentions peripheral neuritis and paralysis of the extremities lasting for months. The meningitis of mumps, while not a common complication, yet occurs often enough to make one employ careful measures during the first two weeks of the disease.

This is an infectious disease, specific and general in its nature, localizing on the salivary glands, but affecting all of the economy. It is the same as the eruptive fevers, of which it partakes in nature, being contagious and epidemic.

CASE REPORTS

CASE 1.—R. S., 11 years old, male, colored, was admitted to the Children's Hospital January 7, 1913, with the following history:

History.—Mother in good health; father alcoholic; one infant brother in good health. The boy was in perfect health up to his present illness, having had none of the diseases of childhood. About Christmas, 1912, the mother noticed that the child's face was swollen, which condition a physician pronounced mumps, of which there was an epidemic. There was fever, no sore throat, appetite good and bowels open. He had frequent desire to urinate but did so with great difficulty. The urine was of a deep yellow color and moderate in quantity. He could not walk without assistance, and complained of much pain in the legs.

Examination.—When he was admitted to the hospital the sides of the face (parotid region) were swollen and there was great swelling and edema of the scrotum (this had come on early in the disease), with marked hypospadia. He took very little notice of surroundings. Lungs, heart and abdominal organs were normal; tongue coated; old ulcer left cornea; child unable to stand; dull and apathetic, but would answer questions in a sluggish manner; pupils unequal in size, the left much larger than the right, but reacted to light; patellar reflexes absent; marked Kernig's sign; no Babinsky.

Course.—January 8. Irritable, complains of pains in arms and cannot turn alone.

January 15. Can roll from side to side in bed, but cannot raise head and shoulders from pillow or sit up. Most of the time is spent in a drowsy state when not actually asleep. Has control of bladder and rectum.

The child up to this time had been on the surgical service, but was transferred to the medical service and came under my charge. A Wassermann made by Dr. W. W. Wilkerson gave a single plus. The first molars were normal.

January 30. Able to sit up.

February 3. Discharge from left ear.

February 16. Examined by Dr. Tom A. Williams. Right patellar reflex feebly present if reinforced; left absent; diadocokinesis not impaired; heel and knee tests negative; ankle-jerk present; can walk and run with eyes closed without incoordination; sense of deep muscular pain absent in limbs, face and neck. Lumbar puncture was made by Dr. B. M. Randolph and the fluid was found clear with no lymphocytosis. The eyes were examined by Dr. D. K. Shute and pronounced normal.

February 27. Examined again by Dr. Williams. Patellar reflex present in left, slightly. Deep pain sense has been recovered.

March 16. Pupils equal in size; no discharge from ear; reflexes normal; child has gained weight and appears well.

This case presents the following features common to many of the cases reported: Fever, pains, delirium, marked Kernig sign, patellar reflexes absent, unequal pupils and paralysis. There was a slow pulse on several occasions, but never a decided bradycardia. The swelling of the scrotum has been noted several times in adults.

Dr. Williams has made the following comments on the case: The absence of deep reflexes and the loss of the sense of pressure-pain, along with unequal pupils and a positive Wassermann reaction, caused suspicion of tabes dorsalis. Loss of the deep pain conductivity is very commonly a symptom in tabetic radiculitis, but the absence of lymphocytosis rendered the diagnosis most unlikely, especially when the onset of symptoms was so acute as in this case. We know that tabes is merely a sequel of chronic syphilitic leptomeningitis, which invariably shows a lymphocytosis until arrested (see Williams: *Am. Jour. Med. Sc.*, August, 1908). But the case is of great interest as a problem of differential diagnosis, which, in the absence of a cytological examination of the cerebrospinal fluid and the history of mumps, could not have been decided for a long time.

CASE 2.—Boy, 3 years of age, entered the service of Dr. Joseph S. Wall at the Children's Hospital April 23, 1913 with the following history:

History.—Father 45 years of age in good health; mother died of tuberculosis nine months previously, 35 years old; otherwise family history good. Birth natural; breast fed for one month only, on account of mother's health. Had always been healthy. Is a well-formed, strong-looking child.

April 14. Complained of pains in the abdomen and had straining of eyes.

April 15. Left side of the neck swollen and the following day the right side became enlarged. Appeared well until April 20, when he became drowsy.

April 22. About 6 p. m. the eyes became set, followed by a convulsion, clonic and then tonic in character, lasting about thirty minutes. Did not regain consciousness until 6 a. m. the next morning.

April 23. Admitted to hospital. Does not recognize anything; cries out as if in pain; vomited milk.

April 24. Right sided convulsions at first, then becoming general, with deviation of the eyes toward the left. Pupils dilated; did not react to light; urine normal; leukocyte count 12,300.

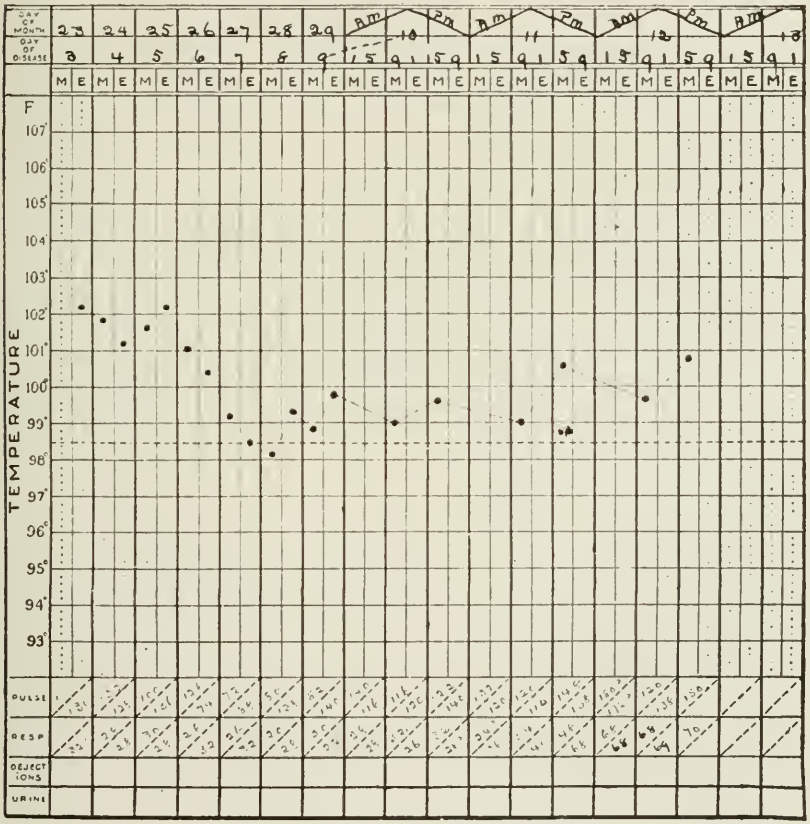


Chart giving data in author's Case 2.

April 25. Very restless, but takes nourishment well. Examination of the cerebrospinal fluid was made by Dr. B. M. Randolph. The fluid came out under great pressure, clear; white cells 90 per cent.; cells mostly lymphocytes; no bacteria found. Leukocyte count of blood 16,500.

April 26. Muscular twitching of face. Pulse was 60 per minute several times during the day.

April 27. Examined by Dr. Tom A. Williams. Reflexes: Patellar, left present; right exaggerated. Ankle clonus present. Babinsky, right equivocal;

left, flexion. Abdominal, left faint; right present. Elbow, left faint; right exaggerated. Deep pain sense present. Motility active. Marked strabismus. Not able to analyze. Pupils dilated; right greater than left; no reaction; tâche cérébrale marked.

April 28. Seemed in stupor the entire night; pulse slow and irregular at times; convulsions during the afternoon involving the entire body.

April 29. Still in stupor. Restless at times; answered "no" to questions. Lumbar puncture made by Dr. Randolph presented the same characters as the last one.

April 30. Eyes examined by Dr. D. K. Shute and found normal. Not conscious; restless; pupils dilated; gnashing of teeth.

May 1. Restless and noisy; difficulty in breathing at times.

May 2. Death.

Necropsy.—Body of male white child, 3 years old. Section made sixteen hours after death. Brain showed marked venous congestion over vertex. There was an increase of serous fluid in the ventricles. Along the base there was a meningitis with a formation of plaques of fibrin. The meningitis did not extend down the cord. On section the brain substance was found normal. Right kidney, stomach and intestines normal, though stomach showed some ptosis. Left kidney, spleen and pancreas showed marked relaxation of their attachments. Pancreas was flaccid and smaller than normal. Pericardium contained small amount of fluid. The lungs were congested and there was a subpleural effusion of blood at base of left lung. There were no areas of consolidation. Bronchial glands normal. No signs of tuberculosis. Mesenteric lymph-nodes enlarged

Anatomical Diagnosis.—Basilar meningitis. (B. M. Randolph, pathologist.)

The following cases of meningitis complicating parotitis have been reported in young persons:

HARVEY LINDSLY: Two cases of death in brothers occurring a year apart, with similar symptoms. The ages are not given, but one was a student at Princeton College and the other a young medical student in this city. The fifth day after the onset of mumps there was persistent priapism in both cases, with delirium, restlessness, convulsions and death within two days. Post-mortem examination in the last case showed "Inflammation and congestion of the cerebellum, the cerebrum being normal."

MOURO AND HEALY: Male, 15 years of age, had mumps (temp. 107.2 F.) with recovery. Suddenly became delirious, hyperesthetic, with coma; maniacal outbreak; orchitis; for six months had difficulty in walking; paresis, and incoordination of legs; difficult speech and marked aphasia.

GLENCREAU: Girl 2½ years old; paralysis right side; convulsive movements at commencement. Recovery in some weeks.

Girl, aged 8 months; light convulsions shortly after the onset of mumps; died within twenty-four hours.

Boy, aged 4 years; extreme restlessness and convulsive movements with the onset of mumps; paralysis of left side.

Boy, aged 5 years. Violent delirium came four days after the onset of mumps. Restlessness with hallucinations. Recovery.

Boy, aged 10 years; severe convulsions with general insensibility; paralysis of left side; marked constipation and difficult micturition. These symptoms lasted a long time.

JOFFROY: Girl, 4½ years of age. The eighth day of mumps, sharp pains in arms and pruritis and afterwards pains in legs. Tendon reflexes and electrical reactions abolished. Hyperesthesia. There was a slight intermittent albuminuria; flaccid paralysis came on twenty-one days after the onset of the disease in the lower extremities and extended to the upper extremities about ten days afterwards. Bladder and rectum normal.

J. R. BROMWELL: Girl, 18 years of age; meningitis; death.

Boy, 11 years of age; four days after the onset of the disease had high fever, delirium, great pain in head, decided intolerance of light, nausea and vomiting. Temperature 104 F., pulse 120. In seven days the patient was well.

ELSAESSER: Three cases. Males from 9 to 11 years of age. Cheyne-Stokes respiration, vomiting, delirium, somnolence, speech disturbance, convulsions, paralysis, death.

COMBY: Boy, 10 years old, presented symptoms of tuberculosis, headache, vomiting, constipation, and rigidity of neck which came on eight days after mumps. Was well in a few days.

NOBÈCOURT AND BRELET: Girl, 12 years of age. On the third day of mumps there supervened headache, vertigo, vomiting, bradycardia, irregular pulse, pupils contracted, Kernig's sign, stiffness of neck and absence of patellar reflexes. At the acme of the disease lumbar puncture showed an abundant lymphocytosis of the clear cerebrospinal fluid which lasted a few days. After a few days the symptoms disappeared without leaving any trace except that the patellar reflexes were feeble for a long time, but became normal.

NETTER: Boy, 9 years old; violent pains in back, kidneys and limbs; Kernig's sign well marked; temperature 40 C. Twenty-four hours later both parotids were swollen. For several days there were brisk movements of the muscles of the face and left arm.

SALAMONSEU: Case 11 years of age. At the end of an attack of mumps there was chorea which lasted for six months and this was preceded by tetany.

J. W. FINDLEY: Female, 2 years of age, had mumps fourteen days. On the sixteenth day became paralyzed after convulsions. Left hemiplegia.

REVELLIOD: Boy, 7 years of age, had mumps with vomiting and fever. In a few days he was apparently well but was weak in left leg. Several weeks afterwards entered hospital; intelligence good; could not stand, rise or hold up head; paralysis of left side of face and eye. Facio-glosso-laryngeal paralysis; all extremities inert; patellar reflexes abolished. In three months recovery with exception of the patellar reflexes.

VAN DUYSE: Girl of 8 years; optic neuritis; violent headache. Later on vomiting and paresis of left side; speech difficult. Sight did not improve.

J. H. WOODWARD: Eleven-year-old child with neuro-retinitis.

BOYREAU: Boy, 11½ years old. February 6. General malaise and headache. Next day there was nausea, vomiting and epistaxis. Temperature 38.8 C., pulse 120. The left parotid became swollen and the following day the right one.

February 10. Could not get up; vomiting; pulse 80; less fever. The next day there was headache, vomiting, constipation, with irregularity of pupils and photophobia. Pulse 58 and irregular.

February 12. Vomiting continued. Pulse 48 and irregular. February 16. Child well.

HUTINEL: Girl, 10 years of age. Facial paralysis.

HEUBNER: Boy, 13 years of age. Psychosis; loss of memory; orchitis; recovery.

H. ZADE: Boy, 12 years of age. Vomiting, chill, slow pulse. Two days later parotitis. Intense headache and other symptoms of intracranial pressure developed. In ten days there was complete recovery.

A. STERN: Two cases of meningeal complications.

Girl, 8 years old. Diplopia due to paresis of the right internal muscle, showing a lesion of some of the fibers of the inferior branch of the third nerve.

Male, 16 years old. Bradycardia, pulse 30 to 38 per minute, headache, extreme dizziness, slight rigidity of the neck, vomiting, loss of appetite and nystagmus. Hearing poor in right ear.

F. L. BENHAM: Boy, 15 to 16 years of age. Mumps and orchitis. Temperature 104 F., pulse 120, vomiting, frontal headache, delirium, tâche cérébrale, stupor.

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DISCUSSION

DR. HOLT: I think such nervous complications of mumps as those reported are interesting because of their rarity. I would like to mention a case of generalized paralysis due to multiple neuritis which I saw two years ago. A child 12 years old, the son of a physician, had had a severe case of mumps. He was sent to recuperate at Atlantic City. Shortly after his arrival there and eleven

days after the cessation of his fever and acute symptoms, he began to grow weak in his legs and in four or five days this increased so that he could take but a few steps. He was at once brought home and I saw him the following day. He could then walk only with considerable assistance; his upper extremities also were weak; knee-jerks were absent; marked tenderness along the nerve trunks and considerable pain in the limbs. In the course of a few days he developed a complete paralysis of the arms and legs. One physician who saw him made a diagnosis of poliomyelitis. There was no fever; the bladder and rectum were not involved. This condition lasted for two weeks, then the paralysis began to improve, and at the end of six weeks' more there was complete recovery. The progress of the case bore out the diagnosis of multiple neuritis. But few similar cases have been reported in literature. With the degree of toxemia not infrequently present in mumps, it is surprising that we do not more frequently see nervous complications. He suggested that some of the cases diagnosticated meningitis might be multiple neuritis. In the case reported the paralysis was precisely like that seen after diphtheria, except for the absence of throat symptoms.

DR. NICOLL: I should like to ask Dr. Acker if a culture was taken in the second case? I do not believe that the causative agent of mumps has been definitely established.

DR. ACKER: An examination has not been made in the second case, but it will be made. The pathologist has not completed his report but a culture and microscopical examination will be made later on and be published with the paper.

TUMOR OF THE CEREBELLUM

SAMUEL S. ADAMS, A.M., M.D.
WASHINGTON, D. C.

B. G., 9 years, colored, Virginia, was admitted to the Children's Hospital, Washington, D. C., Oct. 26, 1912.

Family History.—Father, aged 39, in good health; mother, aged 43, in good health; six other healthy children. Mother has never had any abortions. Family history as to tuberculosis, cancer, syphilis, epilepsy, negative. Mother an alcoholic and father a "drinking man."

Previous Personal History.—Birth normal, breast-fed. According to the mother's statement (she was drunk when interviewed), the boy had never had any of the diseases incident to childhood. He began school one year ago and made good progress during the term.

Present Illness.—About October 1 it was observed that he did not feel well and sat about most of the time, although previously he had been a very active boy. He ate very little, was constipated and had no fever.

EXAMINATION OF VARIOUS SYSTEMS

A fairly well-nourished colored boy lying in bed in stuporous condition; can be aroused, but with difficulty. Does not answer questions well and if not disturbed falls asleep immediately.

Cutaneous System: Skin warm and dry; the right leg is colder than the left; no difference in temperature in the upper extremities. There is a small scar on the forehead; no eruptions on the skin noticeable. Temperature normal, with slight elevations above normal. Glands are not enlarged.

Digestive System: Breath very offensive; teeth in poor condition; the tongue slightly coated; is constipated and passes yellow-greenish stools. The abdomen is apparently normal; some flatulence and distention present; spleen and liver normal size. Patient does not vomit.

Respiratory System: Nose flattened, alae nasi dilated, no dyspnea. Breathing regular. A few moist râles in the supraclavicular and infraclavicular regions; does not cough.

Circulatory System: Normal. The pulse is weak and regular. Pulse 78 to the minute. Blood examination:

Hemoglobin	100 per cent.
Leukocyte count	10,300
Red cell count	6,500,000
Wassermann	++

Osseous system: Normal.

Nervous system: Mentality: Patient is dull and apathetic, but at times is quite rational. Reflexes: Knee reflex absent on the right side, on the left slightly obtainable. Babinski's sign absent. Ankle clonus not obtainable. Ulnar reflex absent. Muscle tone: Both lower extremities are weak; they are not paralyzed, because when asked patient could reflex and extend both legs; he could not flex the feet. Patient is unable to walk and unable to stand unsupported. About two weeks ago patient could walk with the aid of a stick (according to his statement). Muscles of the lower extremities are slightly rigid; wasting is not noticed. Arms are in normal condition, the strength is about the same in both. Muscles of the neck are rigid and the head turns to the right side (torticollis).

Vision: Ptosis marked. Pupils widely dilated, do not respond to artificial light, but he can tell light from darkness.

Ophthalmoscopic examination by Dr. Shute: Left eye shows marked optic neuritis, amounting to choked disk. Right eye shows opacities on account of which the fundus cannot be seen.

Audition is normal.

Hyperesthesia is marked in some portions of the lower extremities. Anesthetic points over the upper extremities and the trunk are detected.

Examination of Cerebrospinal Fluid.—Thirty-five c.c. clear, watery fluid submitted. Protein (Ammon, sulphite method), not increased. Cell count, 5; sugar negative. Cytology: Few small mononuclear cells. Few erythrocytes (traumatism of puncture?). Bacteriological: No micro-organisms found, which includes examination for tubercle bacilli. W. W. Wilkinson, pathologist.

No history of convulsions. Kernig's sign present.

Genito-urinary system: Patient has incontinence of urine. Urinalysis showed urine to be normal.

The boy lay in a condition of stupor for four months with very little change except on one occasion when he was found to be a diphtheria carrier, in company with several other patients, a physician and three nurses. He died March 8, 1913. Necropsy performed by Dr. Randolph.

The treatment consisted of salvarsan, the iodids and supportive treatment. There was no apparent benefit from anything given to him.

Necropsy.—Great emaciation of body and contracture of all the skeletal muscles of the extremities. There are two large sores on each buttock. There is also a large abscess in the right side of head reaching down to the bone, through the periosteum. Heart and lungs normal. The intestinal glands are infiltrated with what appears to be tuberculosis. There is a large tuberculous mass in the mesentery. The brain shows an increase of fluid in the ventricles and in the subdural space. There is a large thrombus in the dural vein. The left lobe of the cerebellum is adherent to the base of the skull. The normal tissue has been destroyed by an inflammatory process, syphilitic or tuberculous, most likely tuberculous.

The tissues from Benjamin Gordon, Case No. 12,819, Children's Hospital, have been examined with the following result:

1920. Cerebellum tumor, tuberculous mass.

1921. Cerebrum, fungoid mass on anterior lobe, pia-arachnoid thickened, fibrous and calcareous.

1922. Mesenteric lymph-nodes, extensive tuberculous mass. F. F. Russell.

Anatomic Diagnosis.—Tuberculosis (solitary) left lobe cerebellum. Edema of the pia. Old pleural adhesions. Tuberculosis mesenteric glands. B. M. Randolph.

DISCUSSION

DR. LUCAS: I would like to ask Dr. Adams if he tried the Wassermann reaction?

DR. ADAMS: Yes; the child had the Wassermann test and had injections of salvarsan but without any apparent effect. I also put her on specific treatment.

EXPERIMENTAL SCORBUTUS AND THE ROENTGEN-RAY DIAGNOSIS OF SCORBUTUS *

FRITZ B. TALBOT, M.D., WALTER J. DODD, M.D.
AND HUGO O. PETERSON, M.D.

I. THE ROENTGEN-RAY DIAGNOSIS OF SCORBUTUS IN INFANCY

FRITZ B. TALBOT, M.D., AND WALTER J. DODD, M.D.

E. Fränkel[1] found certain changes in the bones in infantile scorbutus by the roentgenogram, which he considered characteristic and of diagnostic value. These changes may be found before any of the cardinal symptoms of scorbutus appear, and before there is any evidence of subperiosteal hemorrhage, either clinical or on the roentgenogram.

The characteristic picture is as follows: There is a definite "white line" at the end of the diaphysis at the junction of the epiphysis and the diaphysis on the Roentgen-ray plate or negative. This "white line" appears in the accompanying illustrations (positive) as a "dark line," which runs transversely across the bone as a narrow or broad dark shadow, either in a straight or crooked line. It represents an increased density at the end of the diaphysis. Attention was again drawn to the "white line" by Klotz[2] and Riesenfeld,[3] who both published Roentgen-ray pictures of the bones showing the line. Klotz reports a case of scorbutus in which plates were taken every three weeks after the diagnosis was made and treatment instituted. He found that the "white line" persisted long after there was a complete clinical cure. The line could be seen for three months at the ends of the radius and ulna, and for five months in the tibia and femur after apparent cure.

The writers have seen the "white line" at each end of the humerus, radius, ulna, femur, fibula and tibia. Usually pictures are only taken of the long bones of the legs for diagnostic purposes in actual practice.

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* From the Children's Medical and Roentgenological Departments, Massachusetts General Hospital.

1. Fränkel, E.: Untersuchungen über die Möller-Barlowsche Krankheit. Fortschritte auf dem Gebiete der Röntgen-Strahlen, vii, 231, 291; x, part 1.

2. Klotz: Zur Röntgen-Diagnose des Sauglingskorbuts, Monatschr f. Kinderh., 1908-1909, vii, 36.

3. Riesenfeld: A Case of Scurvy with X-Ray Plates, Arch. Pediat., 1909, xxvi, 128.

The following case serves as an illustration of the diagnostic importance of the "white line":

THERESA K., aged 8 months, entered the children's ward of the Massachusetts General Hospital, Oct. 25, 1912, with the following history: She had always been fed on malted milk and cream in uncertain proportions and had done well. Two months ago the mother heard a "snap" in the right knee while she was pulling on the baby's stocking, and dates the trouble from then. Since that time the baby has been fretful and irritable, especially while being handled, and has not wanted to move her leg as much as she did before the injury. One week ago there was an increase of pain in the legs and rise of temperature without nausea or vomiting or any loss of weight. The physical examination was normal except for the following facts, which are worthy of note: There were no teeth. The gums and mucous membranes of the mouth were of normal color without any trace of redness or swelling. The head was square and there was a moderate rosary and enlargement of the epiphyses of the radii showing a moderate degree of rachitis. The heart, lungs and abdomen were normal. The right leg was held partially flexed, the normal contour being obliterated by swelling which was connected with the middle third of the femur. This mass was hard and smooth and although it was painful to touch, it was not exquisitely so. The right thigh 5 cm. above the patella, was 5½ cm. larger than the left and right calf was 2½ cm. larger than the left. The white count was 8,000, the von Pirquet skin tuberculin and Wassermann were negative. The diagnosis lay between an osteosarcoma, a low grade osteomyelitis and scorbutus. The x-ray showed the typical "white line," thus establishing the diagnosis of scorbutus. Orange juice did not cause any marked improvement for ten days, after which time the improvement was rapid and the child quickly became clinically well. X-rays were taken of the leg about once a month and the "white line" has persisted up to April, 1913, a period of five months. In one instance examined two years after the disease was treated, the "white line" had gone.

The "white line" usually persists for six months after there is an apparent clinical cure of the scorbutus and suggests that, although to all intents and purposes the child is well, the pathological changes persist. The only accurate study of the metabolism of scorbutus in adults has been made by Baumann and Howard,[4] who found that the loss of the various food constituents through the feces was less when fruit juice was added to the diet. The total sulphur metabolism was abnormal throughout the experiment, the quantity eliminated being in excess of that ingested. Chlorin and sodium were retained during the fruit juice period, but were excreted in excess of the intake during the preliminary period. More potassium, calcium and magnesium were retained during the fruit juice period than during the preliminary period. Lust and Kloeman[5] studied the metabolism of nitrogen and the mineral salts in

4. Baumann and Howard: Arch. Int. Med., ix, No. 6.
5. Lust and Kloeman: Jahrb. f. Kinderh., lxxv, No. 6, pp. 663-788.

a typical case of scurvy in an infant 18 months old. Observations were made for three periods of four days each, the first while the disease was at its worst, and the child was not being treated; the second after a month's treatment; and the third a month later, after all symptoms had disappeared. The nitrogen balance was normal at all times. The balance of mineral salts, particularly of calcium, was somewhat increased in the first period; at the second period, during convalescence, it was markedly decreased, and at the third period was approaching, but had not yet reached normal, though the child was clinically well. This is in decided contrast to the conditions in rickets. These works, while impor-

Fig. 1.—Radiograph of Experimental Monkey. Jan. 27, 1913. No evidence of "white line" at diaphyseal junction.

tant, do not explain the persistence of the "white line" after the clinical cure, and further investigation must be carried on to clear up this point.

When scorbutus is associated with rachitis there is in addition to the "white line" a distinct roughening of the ends of the shafts of the bones just as if the end of the bone had been teased out with a needle. There is also the characteristic enlargement always found in rachitis. Plates 1 and 2 illustrate both rachitis and scorbutus, showing both the distinct teasing, enlarged epiphysis and "white line." Rotch (Roentgen Ray in Pediatrics, Philadelphia and London, 1910) shows a plate (No.

79) in which he calls attention to an "irregular zone of proliferation" in a case of scorbutus.

Since presenting this paper, the writers have studied several cases of congenital syphilis. In several of them, some of the bones showed a "white line"; this finding was by no means constant. When the "white line" was present, the babies might also have had a very early scorbutus without any clinical evidence of the disease. In two babies with positive Wassermann reactions the "white line" was absent. Further observations must be made to determine whether the "white line" has any connection with syphilis or rachitis, or whether it is characteristic and is present only in scorbutus.

II. EXPERIMENTAL SCORBUTUS IN GUINEA-PIGS

FRITZ B. TALBOT, M.D., AND HUGO O. PETERSON, M.D.

Practically no observations were made on experimental scorbutus until Holst, Frölich and Von Fürst,[6] Scandinavian physicians, commenced their extensive investigations. Their work has been so complete and painstaking that it is necessary to describe it in considerable detail.

Guinea-pigs were fed exclusively on various forms of bread and grain, and as a result died in four to six weeks of a disease in which the pathological anatomy corresponded with that of human scorbutus. The most common changes were as follows: The teeth became loose, the gums were hyperemic with microscopic hemorrhages, there were extravasations of blood about the costochondral articulations and in the soft tissues about the joints of the extremities. There was frequently subluxation of epiphyses of the long bones, more especially of the upper end of the tibia, and there were characteristic microscopic changes in the bone-marrow. Hemorrhages in the skin were seen less often than in infantile scorbutus. There were frequent hemorrhages into the muscles.

These results have been criticized on the ground that the post-mortem changes and the hemorrhages were due to the inanition of starvation. These criticisms were met by the following experiments: guinea-pigs were fed on fresh white cabbage, dandelions or carrots in such amounts

6. Holst and Frölich: J. Hygiene, Camb., 1907, vii, 619-634.
Holst and Frölich: Norsk Mag. f. Laege., March, 1910, vol. lxxi, No. 3, p. 209-293.
Fürst, V.: Norsk Mag. f. Laege., January, 1912, lxxiii, No. 1.
Holst and Frölich: Ztschr. f. Hyg. u. Infectionskrankh., 1912, lxxii, part 1.

that the animals lost 30 to 40 per cent. of their weight. None of these animals contracted scorbutus, whereas those animals that were fed on dried grains or bread and lost a like amount of weight or relatively a few grams, showed scorbutic changes. These experiments proved conclusively that the scorbutic changes were not due to simple inanition. It is interesting to note in this connection that there are records of cases of human scorbutus which followed a diet which was the same or similar to that given to the guinea-pigs.

Scorbutus in guinea-pigs is relieved or cured by fresh vegetables in the same way as in the human. These antiscorbutic properties are

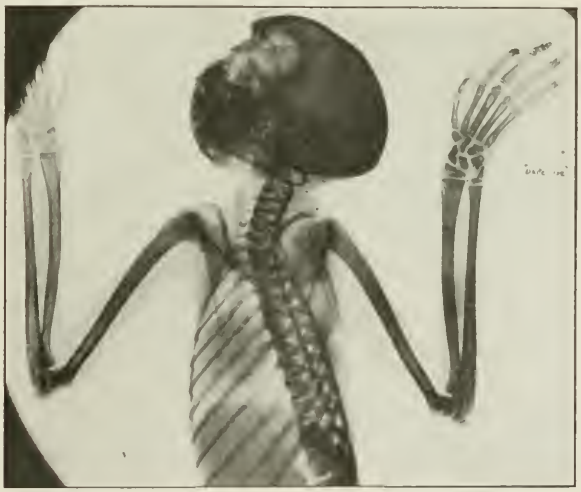

Fig. 2.—Radiograph of Experimental Monkey. April 6, 1913. This plate shows distinct evidence of "white line" at lower diaphyseal junction of radii and ulnae.

usually, if not always, weakened by the process of cooking, yet they are rarely entirely destroyed. There seems to be some connection between the intensity of the heat used in cooking and the loss of the therapeutic properties. For example, white cabbages are of less therapeutic value when they are cooked at 110 to 120 C. than when they are boiled.

The fresh vegetables lose their antiscorbutic properties in varying degrees when they are dried. Among those investigated are potatoes, carrots, dandelions and white cabbage. They are, however, affected differently: dandelions lose their therapeutic value immediately on drying,

while white cabbage retained it longer when kept in an open vessel in an incubator at 37 C. than when it was kept at room temperature. Freshly pressed cabbage juice quickly loses its antiscorbutic properties when it is heated at from 60 to 100 C. for ten minutes. The same thing happens when it is preserved for a long time either at room tempera ture or in an ice-chest. Pressed dandelion juice also loses its prophylactic properties when heated for a short time.

In contradistinction to the above, lemon juice will withstand for a long time the same heat that will weaken or entirely destroy the virtue

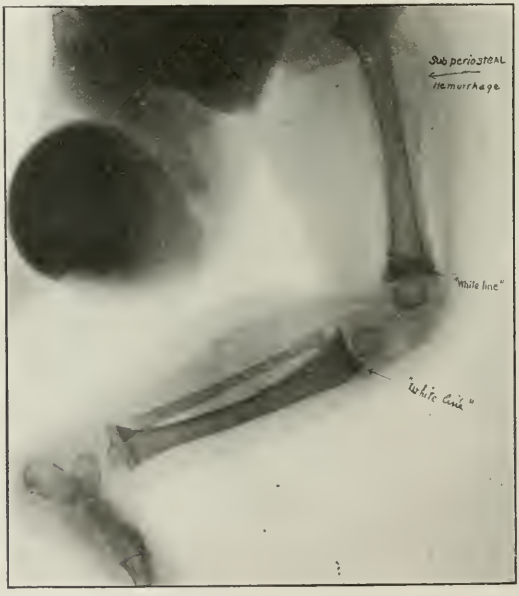

Fig. 3.—Case Theresa K.

of white cabbage or dandelion juice. Raspberry juice can be cooked for one hour at 110 C. without losing any of its antiscorbutic properties. Holst and Fröhlich thought that there must be some connection between the acidity of these juices and their antiscorbutic properties, and they were able to increase the resistance of white cabbage and dandelion juice to heat by the addition of acids. They were not able to increase this resistance so that it would stand prolonged heating. They were unable to determine the nature of the antiscorbutic bodies by dialysis, by extrac-

tion or other experimental methods. Fürst[7] found that feeding guinea-pigs exclusively with plant seeds would produce scorbutus, though not so easily and regularly as with exclusive grain feeding. Plant seeds that produce scurvy would acquire antiscorbutic properties when infected with fungi. He concluded from his experiments that neither the ash nor any of its alkalies plays any part in the incidence of scorbutus. There was no connection between the fat, albumin, carbohydrate, cellulose or enzymes in the food and disease.

Frölich[8] investigated the question of heating milk on the basis that the soluble calcium salts in milk are changed by heat into insoluble cal-

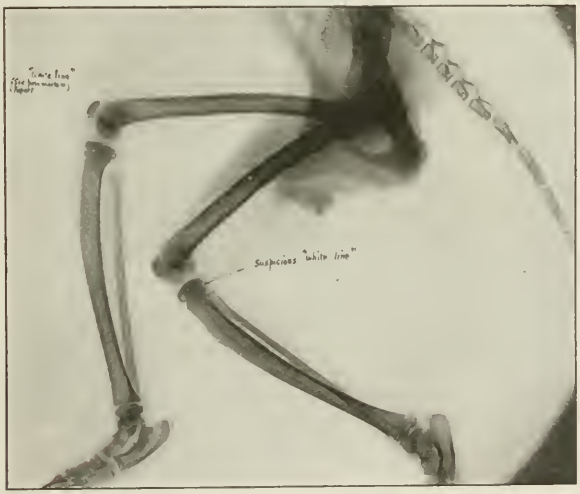

Fig. 4.—Radiograph of Experimental Monkey. April 6, 1913.

cium phosphates, which, according to some investigators, are utilized with more difficulty by the organism.[9] The citric acid in the milk is also changed into insoluble calcium citrate by heat.[10] He found that he could produce scorbutus in guinea-pigs by exclusive feeding with raw or cooked milk, although not so perfectly as by exclusive grain feeding. When fed

7. Fürst: Weitere Beiträge zur Aetiologie des experimentellen Scorbutus des Meerschweinchen, Ztschr. f. Hyg. u. Infectionskrankh., 1912, lxxii, 121.

8. Frölich: Experimentelle Untersuchungen uber den infantile Scorbut, Ztschr. f. Hyg. u. Infectionskrankh., 1912, lxxii, 155.

9. Cronheim and Muller: Biochem. Ztschr., 1908, xi, 76.

10. Obermeier: Arch. f. Hyg., 1, 52.

on oats and raw milk they did not develop scorbutus; when fed with oats and cooked milk they did. Bolle, and after him Bartenstein,[11] tried the effect of heating milk, and found that heating it for a short time had no especial effect on guinea-pigs. When the milk was heated to a high temperature for a long time the guinea-pigs died and single bones showed changes which Bolle identified as scorbutus. Finally the significant experiment of W. Heubner and Lippschultz[12] should be noted. They fed dogs for many weeks on a food poor in phosphorus and found micro-

Fig. 5.—Guinea-pig No. 8. Notice white line. See post-mortem report and microphotograph of the tibia.

scopic changes in the bony system which were very similar to those found in scorbutus.

The work of Japanese investigators may be mentioned incidentally. Okada and Saito[13] and others injected the blood of soldiers suffering

11. Bolle and Bartenstein: Quoted by Hart, Virchow's Arch. f. path. Anat. u. Phys. f. klin. Med., 1912, ccviii, 367.

12. Heubner and Lippschultz: Quoted by Hart, Virchow's Arch. f. path. Anat. u. Phys. f. klin. Med., 1912, ccviii, 367.

13. Okada and Saito: Sei-i-Kwai Med. Jour., Tokyo, Japan, 1905, xxiv, 119, 1906, xxvi, 1.

from scorbutus or cultures from their blood into animals. These experiments do not seem to be free from error and the results add nothing definite to our knowledge of scorbutus.

EXPERIMENTS

The writers undertook to repeat the work done by Scandinavian investigators, both to confirm their results and to obtain experimentally the "white line" by Roentgen ray. The work was as follows: Three guinea-pigs were used as controls and were kept in cages beside the other animals and under identical conditions except for the diet. Three

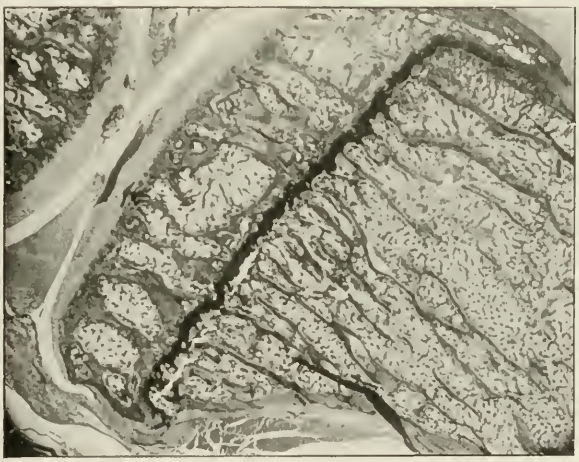

Fig. 6.—Microphotograph. Guinea-pig No. 8. Knee joint, tibial epiphysis. The dark area extending across the bone represents the white line seen by x-ray and is an area of increased density.

guinea-pigs were kept in each cage. The room has been used for guinea-pigs and rabbits for many years without any of them developing scorbutus. It measured 12 by 14 feet, has three windows on the sunny side and two doors which open into corridors. The temperature varies from 75 to 88 F. The control guinea-pigs were fed on bread, oats, grass, carrots, cabbage and water. At the end of eight weeks they had gained weight and were normal in every way. One female produced two healthy offspring.

Eight guinea-pigs weighing less than 250 grams (young animals) were fed on oats or bread and water only and died within ten days with-

No.	Guinea-Pig	Food	Date	Wght. Gm.	Post-Mortem
1	Female ...	Oats and water	Aug. 15	570	Loose teeth. Purple gums. Hemorrhages into the spleen. Died September 14.
			Sept. 8	420	
			Sept. 13	320	
2	Male	Oats and water	Aug. 15	665	Died September 14. Loose teeth. Purple gums. Hemorrhages. Spots in nose and muscle of left hind leg.
			Sept. 3	570	
			Sept. 13	310	
3	Male	Oats and water	Aug. 14	742	Died September 12. Loose teeth. Purple gums. Hemorrhages. Spots in nose and muscle of left hind leg.
			Sept. 5	580	
			Sept. 9	500	
4	Male	Graham bread and water....	Aug. 14	760	Died August 29. Teeth loose. Gums spongy and blue.
			Aug. 19	690	
			Aug. 23	570	
			Aug. 27	485	
			Aug. 28	460	
5	Male	Graham bread and water....	Aug. 14	665	Died September 14. Teeth loose. Gums purple. Urethra hemorrhage.
			Aug. 19	630	
			Aug. 27	620	
			Sept. 3	600	
			Sept. 8	505	
			Sept. 13	380	
6	Male	Graham bread and water....	Aug. 14	451	Died September 14. Hemorrhage in right front leg. Nose, intestines and gums marked stomatitis. Loose teeth.
			Aug. 19	460	
			Aug. 27	400	
			Sept. 3	305	
			Sept. 8	300	
			Sept. 13	210	
7	Male	.....	.....	...	Died in four days, as a result of a fight with another male.
8	Male	White bread and water	Aug. 14	840	Died on September 15. Gums blue. Teeth loose.
			Aug. 19	760	
			Aug. 29	570	
			Sept. 3	550	
			Sept. 8	480	
			Sept. 10	390	
9	Female ...	White bread and water	Aug. 14	640	Died August 28. Teeth loose Gums purple and spongy.
			Aug. 19	590	
			Aug. 23	500	
			Aug. 27	480	
13	Male	White bread and water	Sept. 1	600	Died September 30. Hemorrhagic spots in mucous membrane of stomach and small intestine. Large hemorrhages underneath costal muscles on right side. Teeth dirty and loose, gums purplish and swollen.
			Sept. 7	610	
			Sept. 15	580	
			Sept. 20	560	
			Sept. 30	500	
14	Male	Oats and water	Sept. 1	800	Died September 29. Large hemorrhages in right forearm under muscles and traced to wrist joint. Teeth loose and dirty.
		Water	Sept. 5	810	
			Sept. 15	790	
			Sept. 29	740	
			Sept. 21	780	

No.	Guinea-Pig	Food	Date	Wght. Gm.	Post-Mortem
15	Female ...	White bread and water	Sept. 1	615	Died September 30. Ate nothing during last six days. P. M. hemorrhages beneath muscles of right hind leg. Teeth loose, dirty. Gums purple, not swollen.
			Sept. 5	618	
			Sept. 15	600	
			Sept. 21	580	
			Sept. 29	520	
16	Male	Graham bread and water....	Sept. 1	700	Died October 10. Teeth dirty, not loose. Gums few hemorrhagic areas. Hemorrhages under costal muscles left side.
			Sept. 5	710	
			Sept. 10	600	
			Sept. 18	680	
			Sept. 25	640	
			Sept. 30	630	
			Oct. 5	600	
			Oct. 10	580	
17	.....	Oats and water	Sept. 1	410	Died October 5. Spongy hemorrhage gums. Teeth dirty. Not loose.
			Sept. 6	415	
			Sept. 12	400	
			Sept. 24	380	
			Sept. 29	365	
			Oct. 5	320	
18	Male	White bread and water	Sept. 1	482	Died September 29. Teeth dirty. Right foreleg hemorrhagic.
			Sept. 4	481	
			Sept. 10	472	
			Sept. 20	460	
			Sept. 28	400	
19	Male	White bread and water	Sept. 1	565	Died October 12. Teeth dirty. Gums purplish.
			Sept. 4	560	
			Sept. 6	550	
			Sept. 20	542	
			Sept. 30	536	
			Oct. 12	522	
	Control guinea-pigs			10	11 12
			Aug. 14	600	820 grams. 450 grams.
			Aug. 20	610	820 grams. 450 grams.
			Aug. 28	610	822 grams. 452 grams.
			Sept. 4	612	822 grams. 452 grams.
			Sept. 10	615	825 grams. 455 grams.
			Sept. 20	615	825 grams. 455 grams.
			Sept. 30	615	830 grams. 458 grams.

out showing any scorbutic changes. The Scandinavian investigators had the same experience. These young guinea-pigs, therefore, cannot stand the stress of such a rigid diet long enough to show any pathological changes which can be considered scorbutus.

The other eighteen guinea-pigs were divided into three lots, one of which received oats and water alone, another rye bread and water alone, and the third white bread and water alone. During the first week they

ate the food greedily and gained slightly in weight. After that they began to lose weight. After the second week they would sit still in one corner of the cage instead of running about as formerly, and they would not eat unless the food was put directly in front of them. At the beginning of the third week the teeth of some of the animals became loose, and the gums swollen and hemorrhagic, bleeding easily at the slightest touch. When they walked they limped as though protecting a painful extremity.

They became emaciated in four to five weeks; the spine was very prominent and they looked shriveled up. Death occurred in thirty to forty-five days.

Guinea-pigs Nos. 20 to 28, inclusive, weighing, respectively, 200 grams, 180, 230, 240, 211, 206, 190 and 198 grams, all died within ten days.

The following macroscopic pathological changes were found at post-mortem: The teeth were loose and of a dirty gray color instead of the healthy pearly white luster. The gums were hyperemic or purplish and swollen. There was increased fragility of the bones and hemorrhages into the muscles of the legs in many animals. In one instance it was traced to the periosteum near the epiphyseal line of the ulna. In another there were small hemorrhages into the mucous membrane of the stomach and small intestine.

The following pathological reports were made by Dr. N. Chandler Foote:

GUINEA-PIG 1.—Humero-ulnar and femoro-tibial articulations examined.

Grossly.—Numerous intramuscular hemorrhages in the neighborhood of the bone; a few scattered subperiosteal hemorrhages.

Elbow.—Periosteum and bone negative. Bone marrow very much congested, with occasional focal hemorrhages. (Of these some fresh, some several days old.) Occasional hyalin thrombi in vessels. No rarefaction of marrow. No epiphyseal lesions.

Knees.—Extensive subperiosteal hemorrhage about upper end of tibia, with large number of pigmented wandering connective-tissue cells. Diffuse round-celled infiltration of periosteum and peri-articular soft parts. Bone marrow for the most part intact; in the cancellous portion of the bone of the head of one tibia is an area 2 by 2 mm. of rarefied marrow, composed of a fine reticulum of young connective tissue, fibro-blasts, round cells and marrow cells, with a bluish, granular, myxomatous material between them. This is just distal to the epiphyseal line in the upper end of the shaft. The epiphysis is somewhat ragged and eroded in appearance. The other knee duplicates the condition throughout.

GUINEA-PIG 2.—Knee and shoulder joint examined.

Grossly.—There are a few subperiosteal hemorrhages, many intramuscular extravasations in the soft parts about the joints.

Knee.—Marked intramuscular hemorrhages, microscopic subperiosteal hemorrhages about the shaft of the tibia throughout its uppper two-thirds. Marked round-celled infiltration of the peri-articular soft parts. The structure of the bone marrow is normal, but the organ is markedly congested, with numerous focal hemorrhages into its substance. There is a slight leukocytic exudate into the joint-cavity.

Shoulder Joint.—Shows the same conditions, but the peri-articular infiltration is less marked. There is slight infiltration and thickening of the periosteum.

Opposite Knee.—There is very marked subperiosteal hemorrhage about the tibia with equally marked extravasations into the soft parts. The bone marrow, aside from scanty localized hemorrhage, shows nothing abnormal. Epiphysis in every case normal.

GUINEA-PIG 4.—Both knee joints.

Grossly.—Moderate subperiosteal and intramuscular hemorrhages.

Microscopically.—Periosteum everywhere thickened, with extensive extraperiosteal hemorrhages overlying it. Over the upper end of the shaft of the tibia there are spaces under the periosteum, where osteoclasts are situated and where these have eroded the subperiostal surface of the shaft until it is very ragged in appearance. In such areas there is a concomitant infiltration by round cells and occasionally polymorphonuclear leukocytes. The bone marrow is everywhere markedly congested and rarefied, the lymphoid character of the organ being retained only in the immediate vicinity of the blood vessels or sinuses. There is much bluish granular mucoid material in the rarefied portions, embedded in which are fibroblasts and other young connective tissue cells, which form a reticulum far more delicate than was the case in Guinea-Pig No. 1. The entire bone marrow is involved in this process here. There is some rarefaction of the beam work of the cancellous portion of the head of the tibia and the shaft below the epiphysis. The latter is dense and eroded on its under surface. In one place it is markedly thickened and its cartilage cells irregularly formed and distributed. The femur shows a similar process, but to a lesser extent and there is no subperiosteal resorption going on its case.

The bony members of the other knee joint show less absorption in the cancellous tissue. The femur shows more periosteal thickening and infiltration than does its fellow. Occasional minute subperiosteal hemorrhages are to be found. The marrow is in every way analogous to that of the bones of the opposite side.

GUINEA-PIG 5.—*Grossly.* Scanty hemorrhages located almost entirely in the muscular tissue. Both knees examined.

Microscopically.—The femora show no subperiosteal hemorrhages or periosteal thickening of infiltration. The marrow of the shaft is normal, that of the condyles shows a few areas of early rarefaction, with very little of the myxomatous, bluish intercellular substance. Usually the reticulum lies in a clear homogeneous medium and is extremely delicate in its structure. In the tibiae the same condition obtains. The epiphyseal cartilage is normal in every case.

GUINEA-PIG 6.—Grossly. Slight intramuscular hemorrhages. Both knees.

Microscopically.—The right femur shows extensive, old and almost absorbed subperiosteal hemorrhage, extending along the shaft. The periosteum is thickened and infiltrated, with many polymorphonuclear leukocytes. The bone marrow is congested, but normal. Epiphyseal cartilage normal, regular, not eroded. In the other knee there are similar conditions, excepting that there is marked rarefaction of the marrow of the head of the femur, distal to the epiphysis, and moderate myxomatous change. There are none of the subperiosteal hemorrhages, as noted on the other side. There is, however, marked thickening of the periosteum, with infiltration and swelling of its tissue.

GUINEA-PIG 8.—*Grossly.* Slight intramuscular hemorrhages at both knees and hip on one side.

Microscopically.—Marked subperiosteal extravasation about the head of the tibia, near the joint surface. Marked infiltration of periosteum and muscle in vicinity of the femur, without hemorrhage. Moderate medullary rarefaction without any myxomatous deposits.

Other Knee.—As above, but with some myxomatous deposit. The femoral epiphysis somewhat thickened and of irregular construction, the *tibial dense and eroded* (see microphotograph and compare with radiograph). The subperiosteal surface of the tibia is rough, but no active resorption is going on. The head of the femur shows medullary rarefaction without other lesions, save hemorrhage into the muscle in the neighborhood of the joint.

GUINEA-PIG 9.—*Grossly.*—Marked hemorrhages into soft parts.

Microscopically.—Marked hemorrhage into the tissue about the knee, though no true subperiosteal hemorrhage is to be found. The soft tissues are infiltrated and swollen. The marrow is normal, contains much fat and is moderately congested. The bone of the opposite knee joint is normal in every case. All the epiphyses are regular and normal in appearance.

The gross pathology in all the guinea-pigs and the microscopic pathology in all those examined, except No. 5, show the characteristic changes of scorbutus. Animal No. 5 may have had a very early scorbutus which did not have time to develop the microscopic changes. It did have the clinical manifestation of scorbutus in loose teeth and purple gums.

In the majority of instances the x-ray showed that the epiphysis and diaphysis had joined and there was no evidence of the formation of the "white line." The very young guinea-pigs whose epiphysis and diaphysis had not joined, died before there was any evidence of scorbutus. Guinea-pig No. 8 (see accompanying radiograph) shows a definite though slight "white line" at the upper diaphyseal junction of the right tibia. This appears as a dense area in the microscopic section and corresponds with the "white line" in the radiograph.

III. EXPERIMENTAL SCORBUTUS IN THE MONKEY

WALTER J. DODD, M.D.

Scorbutus is not a spontaneous disease which appears under natural conditions in animal life, because Nature supplies the animal world with fresh food. It is, therefore, only under exceptional conditions that the young and growing animal will be given a diet which will cause disease.

A baby is naturally fed at the breast and it is doubtful whether scorbutus ever develops under those circumstances. When it is fed on one of the proprietary foods or boiled milk, scorbutus often develops. The experiments reported below were undertaken to determine whether scorbutus would develop in the monkey if one of the proprietary foods were given and also to cause the formation of the "white line."

In March, 1911, Hart[14] fed a young monkey on trade condensed milk and kept it in such surroundings that it did not become rachitic. It eventually died with typical scorbutus, while the control monkey which received a mixed diet did not. The earliest symptom observed was bleeding of the gums; later the molars became loose. None of the teeth fell out and there was no ulcerative stomatitis or hemorrhages into the skin. There were hemorrhages accompanied by swelling and pain either in the knee, hand or foot. In another instance exophthalmos with an edematous hemorrhagic swelling of the upper eyelid appeared suddenly. Abnormal crepitus during life was found to be due to fracture at post-mortem. Bloody diarrhea was a frequent occurrence, while hematuria was not observed. He found the "white line" by Roentgen ray.

The above experiments were repeated by the writers in the following manner:

Two young Java monkeys, aged approximately six months each and about the same size were placed side by side in cages in a warm, airy, clean room where they could obtain plenty of exercise. The female or control animal was fed on cow's milk, carrots, raw apples, bread and bananas. At the end of the period of observation she was healthy and strong and showed no signs of rachitis. The male animal was fed on one of the common brands of condensed milk. Both monkeys were kept under observation for some time before the experiment was commenced. The diet of condensed milk was started on Jan. 6, 1913, and was taken well for several days. Later the monkey lost his appetite and would only take it when hungry. The stools changed rapidly from the normal reddish color, became yellow and eventually shiny, like the white of an egg. The character of the urine changed so that after the diet had been given several days there was no odor of ammonia in the male monkey's cage, whereas it was very marked in that of the female. There was no appar-

14. Hart: Ueber die experimentelle Erzeugung der Möller, Barlowschen Krankheit und ihre endgültige Identifizierung mit dem klassischen Skorbut. Virchow's Arch. f. path. Anat. u. Phys. und f. klin. Med., 1912, ceviii, 367.

ent change in the condition of the male for eight weeks except that his appetite became very poor, and it seemed wise to give him a little dry bread and boiled milk because he developed a diarrhea. As soon as possible (about forty-eight hours) unsweetened condensed milk was substituted for the boiled milk and the sweetened condensed milk. He then began to show the effect of the diet; he would sit on the floor of the cage with his head between his front paws and would raise his head with much difficulty. His face and ears showed signs of a marked anemia. Finally it was necessary to feed him forcibly with the bread and condensed milk. On March 29 the gums around the two upper middle incisors became purplish red and spongy, but there was no tenderness around the bones or evidence of subperiosteal hemorrhages. Seven days later, April 5, the redness had extended to the first molars and the part first affected had become ulcerated. He died on April 6, exactly three months after the condensed milk was started and nine days after the redness of the gums was first observed.

The pathologic report is as follows (by Dr. Chandler Foote):

MONKEY.—Rhesus Macaque, 45 cm. in length.

Eyes.—Sclera totally obscured by discolored, subconjunctival hemorrhage.

Mouth.—Numerous hemorrhagic ulcerations of both upper and lower gums, involving the frenum of upper lip. Teeth not loosened.

Abdomen.—Abdominal fat reduced in amount, of a butter-like appearance.

Diaphragm at normal level, liver does not present. Intestines in normal position, collapsed.

Thorax.—Shows no abnormalities in situs of contained organs.

Viscera.—Heart normal in every respect save for its epicardium, which is spotted with innumerable punctate hemorrhages, which are distributed over the right heart, roots of the large vessels and extend into the myocardium for a short distance. Microscopically they are the only discoverable lesion aside from slight cloudy swelling.

Lungs.—Show marginal hemorrhages at their lower anterior borders; otherwise normal. Confirmed microscopically.

Mediastinum shows numerous hemorrhagic foci.

Organs of Neck free from lesions.

Liver shows generalized fatty infiltration and slight hemosiderosis, the latter seen only under the microscope.

Spleen shows marked hemosiderosis and some congestion. Infective splenitis ("septic spleen.")

Pancreas normal.

Stomach Normal.—Small intestines show marked mesenteric hemorrhage, but are otherwise normal. Colon is the seat of a well developed ulcerative colitis, the ulcers in some cases extending completely around the gut, having sluggish,

everted margins and eroded, hemorrhagic bases. The mesocolon is the site of enormous hemorrhages between its two layers.

Kidneys and genito-urinary apparatus intact.

Skeleton.—Aside from slight hemorrhages into the serous ligaments of the joints (ligamentum teres at hip, ligamenta alaria at knee, etc.), the bones show no lesions in the bone marrow. There are no subperiosteal hemorrhages, no medullary hemorrhages or areas of gross rarefaction. Microscopically, the epiphysis in the lower end of the right femur (see radiograph) shows localized denseness extending into the epiphyseal cartilage for approximately one-quarter of its total thickness. Wrist-joint, where "white line" was most evident in the radiograph, not examined owing to misunderstanding.

Anatomical Diagnosis.—Ulcerative stomatitis. Extensive ulcerative colitis (chronic, hemorrhagic). Multiple hemorrhages into conjunctivae (bilateral, complete), epicardium, anterior mediastinum, lungs (slight), mesocolon, mesentery, synovial ligaments of knee, hip, shoulder and elbow joints. Fatty infiltration and hemosiderosis of liver. Marked hemosiderosis of spleen, with slight splenitis.

Cause of Death.—Chronic ulcerative colitis.

NOTE.—The condition is suggestive of infantile scurvy when considered with the clinical history of the case. There is, however, no definite proof that this disease was present. The findings in the bones were negative throughout both for rachitis and scurvy.—N. C. F.

During the period of observation radiographs were taken of the animals to determine any changes in the bones and to find the "white line" and the time of its appearance. No lesions were observed on the radiographs taken during life. The plate taken just after death shows a slight but definite increase in density, i. e., a "white line" at the diaphyseal junction of the lower end of each radius and a suggestion of the same thing at the lower end of the ulna. There is also a thin but clear "white line" at the lower end of the right femur. This plate is a much better radiograph than those taken during life and has much more contrast. This additional contrast does not in our opinion explain the increased density at this point.

SUMMARY

The "white line" on the radiograph is a constant sign in infantile scorbutus. It may persist many months after there is a complete clinical cure, suggesting that the pathological changes in the bones are not repaired for many months and that the repair is very slow.

Scorbutus may be produced experimentally in the guinea-pig and in the monkey. Although our monkey was clinically scorbutic, the pathological findings were *not* characteristic. Hart's monkey showed both clinical and pathological changes characteristic of scorbutus, and we feel,

therefore, that it is safe to say that scorbutus can be produced experimentally in the monkey. The "white line" can be produced experimentally in both the guinea-pig and the monkey; this line is seen under the microscope as a localized area of increased density.

DISCUSSION

DR. HOWLAND: I should like to ask wherein the white line in scurvy differs from that which is seen in syphilis. In syphilis the excess of calcium at the junction of cartilage and bone gives a satisfactory explanation for the increased density which is found there. The characteristic pathological changes in scurvy are in the marrow, hemorrhages and substitution of loose meshed connective tissue for the usual marrow cell. It is hard to see how such structures would cause a shadow.

DR. HEIMAN: It was formerly the general belief that scurvy was due to sterilized foods, or the absence of fresh foods from the diet. At present the consensus of opinion is that scurvy is due to imperfect metabolism. The condition is analogous to that of beriberi, in which the ingestion of polished rice leads to the production of polyneuritis, as a result of the absence of substances supplied by the husks. When the husks are added to the diet the patients improve.

DR. NORTHRUP: I would like to ask Dr. Talbot if he really feels in his innermost mind and to his best judgment that this is a reliable test, after having made experiments with controls in infants of equal age, free from rickets? If he thinks it is reliable, and whether he does not feel there is in all these cases rickets present.

DR. TALBOT: The white line under the microscope takes on a very deep blue stain which the pathologist thinks very different from the blue stain in the normal bone and which is supposed to represent increased density. In answer to Dr. Heiman, I was under the impression that beriberi was due to lack of substance found in the husks of the rice grain. In answer to Dr. Howland, I have yet to see white lines in hereditary lues. We believe it is one of the important signs of scurvy, although it may be present in rachitis.

STUDIES IN CARDIAC STIMULANTS*

I. STRYCHNIN AND CAFFEIN GROUP

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In considering the therapeutics of cardiac conditions in children, one is rather surprised to find that therapeutic measures have either been handed down or accepted simply from pharmacological experimentation, which is not always an accurate estimate of the clinical value of any therapeutic procedure or of any drug. It is interesting to note the paucity of material which deals with accurate observations of the different drugs used in cardiac conditions. Practically all of the English text-books speak of digitalis and strychnin as the two cardiac stimulants of choice. Digitalis has been tested out both experimentally and clinically, so that there can be very little doubt as to its value.

In regard to strychnin, there is conflicting evidence from the side of the pharmacologist and that of the clinician.

It is still further interesting to note that in none of the German text-books is strychnin mentioned, and it is very seldom used except in America and England. In this country it has been accepted, and it has probably the widest use of any cardiac stimulant.

From a pharmacological standpoint, the effect of strychnin is on the sensory centers, not motor. "The action of strychnin," as stated by Dr. Sollmann, "consists in facilitating the passages of the nervous impulses through the sensory paths so that very slight stimulation leads to exaggerated motor responses." Strychnin in small doses increases the reflex excitability of the spinal cord, so increasing the muscle tone, which in itself brings about certain secondary results, such as (1), increased metabolism; more oxygen is consumed and the CO_2 output is increased, as is also the glycogen consumption increased; (2), there is a tendency to a rise in blood-pressure and an increase in the pulse-rate; (3), temperature is increased. Strychnin causes a stimulation followed by depression of the medullary centers, particularly the respiratory and vasomotor centers. Its effect on circulation in small therapeutic doses

* This paper was written from the wards of the Boston Dispensary Children's Hospital.

is a direct action on the vasomotor and vagus centers, and an indirect action by convulsions, respiratory movements and asphyxia. The action of strychnin on the heart is at first stimulation; but this is only seen when the heart is directly perfused with a strong solution, and it cannot be considered, therefore, as a cardiac stimulant in any therapeutic manner. Indirectly, strychnin may improve the circulation by improving the respiration, or by altering the distribution of the blood without affecting the general blood-pressure. In large doses, it has a marked effect on the circulation. There is a marked rise in blood-pressure due to central vasomotor stimulation aided by convulsions and asphyxia. The respiratory center is stimulated by strychnin, both directly and reflexly, through increased muscular work. Its effect on the respiratory center is important. It removes the depression of the respiratory center. "It should not be used in heart diseases, for if it has any action it increases the work of the heart."[1] The action of strychnin on the respiratory center evidently is much more certain than its vasomotor effect, where the respiratory failure is due to depression or fatigue. Further, Dr. Sollmann says: "Its value is as a temporary bridge; it does not permanently improve the condition of the nervous system; it simply increases its irritability." Such is the opinion of one of the foremost pharmacologists of this country.

From clinical studies we have diversified findings. Hirschfelder[2] made some tests on normal persons with normal hearts, and found that with doses as high as ¼ of a grain hypodermically there was no effect on maximal or minimal pressure, pulse-rate or respiration; and from single doses, scarcely any increase in reflexes. Hirschfelder quotes Dr. P. D. Cameron on some experimental tests that he made on the effect of strychnin on cardiac tonicity. Cameron found 1/4,500 grain per pound, or .00003 grams per kilo, which corresponds to about 1/30 grain hypodermically for a man, always produces an increase in the tonicity of the heart muscle, though without affecting the force of the beat or markedly changing the maximal pressure. The mean and minimal pressure are usually slightly increased by 10 to 15 mm. mercury, and usually the pulse-rate was a little slow. Larger doses increase the systolic output, raise the blood-pressure, slow the heart and increase the tonicity. Hirschfelder[2] further says (p. 181) that strychnin stimulates

1. Sollmann: Text-book of Pharmacology, p. 159.
2. Hirschfelder: Diseases of the Heart and Aorta, p. 182.

both the vasomotor and vagus centers, hence raises the blood-pressure and slows the pulse-rate.

In 1903, Henry W. Cook,[3] and Henry Cook and John B. Briggs[4] give their observations on the clinical value of Blood-Pressure. They say:

> Strychnin was found to have a more positive effect on the blood-pressure. Hypodermic doses of 1/400 of a grain for infants, and 1/200 of a grain during the second year, and 1/100 during early childhood as a rule produced a rise in blood-pressure in ten to twenty minutes, which was well maintained for two to six hours as long as the child was not moribund. Children that do not need stimulation do not show these marked responses to strychnin, nor do the moribund when the vasomotor center is insensitive to stimulants. It is the large intermediate class of toxic and marantic conditions accompanied by low tension pulse-pressure met with in pediatrics where carefully regulated stimulation is so satisfactory in its beneficial results.

Cook and Briggs, working with adults, state that strychnin given hypodermically in doses of 1/60 to 1/10 of a grain produces a rise in blood-pressure, the onset of which is somewhat delayed as compared with that sometimes seen following the administration of alcohol by mouth, whose increase is not so abrupt, but which is maintained for a much greater length of time, varying in average cases from one to four hours. This rise in blood-pressure is distinctly seen to be accompanied, in the majority of patients carefully observed, by an improvement in the patient's general condition. Again:

> On the whole, strychnin is by far the most satisfactory cardiac stimulant for long routine administration, the maintenance of a satisfactory blood-pressure level free from intervals of depression being most easily accomplished by its use in appreciable doses.

They found a rise in blood-pressure from 80 to 120 mm. Hg after 1/20 grain not extraordinary. They believe in starting with large doses when there is a low pressure, and sustaining the increase which they obtain with smaller doses at regular intervals. They give three groups of cases in which strychnin in moderate and large doses fails to raise the arterial blood-pressure: (1), moribund cases (in the following work there are none of this class); (2), cases not really in need of stimulation — relatively normal individuals; (the question might be raised whether cardiac cases can be classed in this group; if so, perhaps the cases which

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3. Cook, Henry W.: Clinical Value of Blood-Pressure Determinations as a Guide to Stimulation in Sick Children; Am. Jour. Med. Sc., cxxv, p. 433, and Johns Hopkins Bull., Feb., 1903, p. 38.

4. Cook, Henry W., and Briggs, John B.: Clinical Observations on Blood-Pressure, p. 512; Johns Hopkins Hosp. Rep., 1903, ix.

follow might be said not to have needed stimulation); (3), cases in which the blood-pressure is already being maintained at stimulation level of the individual case. In these three groups, they found that a single dose usually had no effect. Their findings are in marked opposition to the statements which Sollmann made: that strychnin is "only to be used to bridge over some acute respiratory or cardiovascular failure; not for continuous use, and that it is not a cardiac stimulant."

Dr. R. C. Cabot[5] used strychnin in thirty-one cases of typhoid fever, four cases of pneumonia and fifteen cases with a variety of diagnoses. He gave a total daily dose of about 1/8 grain, but sometimes 1/6. He took 5,000 blood-pressure measurements, and comes to the conclusion that the total result was negative. He says, "I have been unable to convince myself that strychnin exerts any influence on the blood-pressure in febrile cases when given in the doses as mentioned."

James McKenzie[6] states, "Strychnin acts probably on the nervous system, and by producing some exhilaration proves useful in cases in which a temporary exhaustion causes distress. But it cannot be too strongly insisted on that, though it is commonly employed in extreme cases of the most diverse kind — for instance, where there is a sluggish ventral contraction in heart-block — its usefulness is very doubtful and of a limited kind, and should not be relied on in cases of real heart exhaustion."

David Marvin,[7] in giving the results of some clinical observations which he had made with strychnin on medical students, says: "I believe that this evidence, obtained from thirty observations with varying doses, is conclusive proof that strychnin when given in the above doses by hypodermic injections, does increase blood-pressure in the normal man," the doses being 1/40, 1/30 and 1/20 gr. He found no appreciable effect on the rate of respiration; he found that the pulse-rate was slowed five beats from 1/40 gr.; that the pulse-rate was slowed seven beats from 1/30 gr., and the pulse-rate was slowed eight beats from 1/20 gr. The maximum effect was reached at the end of forty minutes from 1/30 and 1/40 gr.; the effect of 1/20 gr. lasted several hours. The pulse-pressure showed an increase of 3 mm. Hg from 1/40 gr., 13 mm. Hg from 1/30, and 8 mm. Hg from 1/20 gr. His conclusions are that there is no effect on the respiration; there is a slowing of the pulse from all doses; a

5. Cabot, R. C.: Proc. Assn. Am. Physicians, 1904, p. 22.
6. McKenzie, James: Hare's Modern Treatment, ii, 123.
7. Marvin, David: Arch. Int. Med., 1913, vii, No. 4, p. 422.

marked increase in blood-pressure from a thirtieth and a twentieth of a grain, and practically none from a fortieth.

L. H. Newburgh,[8] in some work carried out this past year (1913) at the Massachusetts General Hospital on patients suffering from cardio-vascular conditions, found that strychnin given in the ordinary doses has no effect on blood-pressure, pulse, respiration, cardiac conditions or in the way of general improvement.

The only observations on children are those by Cook previously referred to. He states that the blood-pressure during the first few months of life is from 70 to 75 mm. Hg; from six to twelve months, 80 to 85; that below 60 is rare during the first year, except in cases in which there is marked need for stimulation. During the second year, the blood-pressure ranges from 80 to 90 mm. Hg; during the third year from 90 to 100, and from the third to the tenth year, 85 is moderately low, 75 is low and 65 very low. He found that crying and restlessness raised the blood-pressure 5 to 10 mm. Hg. He found that the highest pressure occurred between 4 and 7 o'clock at night, and the lowest probably between 3 and 7 a. m. My experience agrees with these findings. In his cases, all of whom were infants, there were no cardiac cases. Judging from his charts, strychnin was usually used in conjunction with, or followed very closely by, digitalis; and if the two were separated, it was not enough so as to be able to separate their effects. In his Chart 5 there is, in fact, a fall of blood-pressure after strychnin instead of a rise, the rise occurring after digitalis. In Chart 6 there is a rise of 10 mm. Hg after strychnin in comparatively small doses. This was not a cardiac case.

I have been able to watch the effects of strychnin in nine cases during the past few months. All these cases were the result of endocarditis occurring in the course of rheumatic fever infection. The methods of carrying out the observations were mainly as follows (the detailed account will be found in the protocol of each case):

After admission to the hospital the children were given very little or no medication the first few days, sometimes for longer periods, to see what effect the rest would have on their general and cardiac condition. They were then given some one of the cardiac stimulants for a definite period. Some of the cases were put on digitalis, and kept on this drug for several weeks before a trial of strychnin was made; and while the strychnin was being given, the patients received no other cardiac stimu-

8. Newburgh, L. H.: Paper read before the New England Pediatric Society, March 29, 1913, as yet unpublished, so no direct quotations are possible.

lant. Strychnin was given for a period of from two to four days, in varying doses, and its effect watched closely and compared with their average picture as relating to cardiac condition, pulse, respiration, blood-pressure, also their general improvement, appetite, freedom from pain, improvement in restlessness, etc., when simply resting in bed or resting in bed plus digitalis. In this way, it was hoped that some conclusions as to the effect of strychnin in such cases could be fairly accurately made. I very quickly found that strychnin is practically of no avail when given in the ordinary doses which are prescribed for children. (See J. P.'s chart.) Even in adult doses of 1/50, 1/40 or 1/30 gr., there were no appreciable effects. It was only when doses amounting to 1/10 grain or more were given (either at one dose or in quick succession of smaller doses) that any appreciable effect was noted; and then the effect appeared within thirty minutes and disappeared within two hours.

In four cases in which I have studied caffein sodium benzoate as a stimulant, and which I am carrying on further at present, in the ordinary dose of ¼ or ½ grain hypodermically or by mouth, I could observe no effect; only in doses of two or more grains hypodermically was there any appreciable effect, and then the effect was very small and of short duration. (See Charts 4, 12, 15, 16, 17.)

From these observations I conclude that strychnin and caffein in the doses usually used for cardiac stimulation are of no value. It is only when the larger, maximum doses are used that we get any effect, and the effect is usually then of short duration. Whether this is a beneficial effect is even questionable in children with cardiac involvement. It may well be, as Dr. Sollmann suggests, that strychnin stimulation makes the heart work harder, and that it should not be used as a cardiac stimulant. Its effect on respiration in the conventional dosage is of no value; in larger doses, it does appear to slow the respiration up to the point where there are toxic symptoms (slight twitchings) of increased hypersensitiveness of the reflex arc, or when the heart action becomes more rapid and the blood-pressure falls.

CASE REPORTS

CASE 1.—Margaret M., aged 15 years, hospital No. 1198, admitted April 27.

History.—Family history is negative. Patient had had measles and whooping-cough. She was subject to frequent sore throat. She had the first attack of rheumatic fever one year previously. She was treated in the out-patient department for several months and improved until she started to school in September. She grew gradually worse until in October when she was sent to a convalescent home. There she remained until she was admitted to the hospital, April 27.

She had been doing well until a week before admission when she contracted severe tonsillitis with high temperature. The temperature ran as high as 103 F. Her cardiac attack became markedly worse; there were marked dyspnea and precordial pain.

Physical Examination.—Physical examination showed a well developed but poorly nourished girl; very pale, with marked dyspnea and slightly cyanotic. She had an anxious look. Her throat was injected and her tonsils were large; there was no exudate. There was a marked precordial bulging and precordial pulsation was visible throughout the anterior thorax. Apex beat was in the sixth interspace 2 inches outside the nipple line. The left border was in the mid-axillary line. The right border was 4 cm. from the mid-sternal line. Heart action was very irregular. The sounds were weak and both systolic and diastolic murmurs were present. It was impossible to get an accurate blood-pressure reading.

Patient was put to bed and given ⅛ gr. morphin, and ice bags were applied to her heart. She was nauseated and vomited easily. Her pulse on admission was 120; respirations 30. By May 2 the patient had quieted down considerably, the pulse remained between 80 and 90, and respirations between 20 and 30.

Cardiac Condition.—If anything her heart was more irregular and her pulse was fuller. Cardiac area was the same size as on admission. She received ⅛ gr. morphin as needed for pain two or three times in twenty-four hours.

On May 2 strychnin was given, 1/30 gr. by mouth every three hours. Her blood-pressure on May 2, before starting strychnin, was between 95 and 100 mm. Hg. It was very hard to read accurately.

May 4 her respiration ranged between 22 and 26, radial pulse between 112 and 120; apex pulse-rate between 130 and 140. Blood-pressure on May 4 at 12 o'clock noon was 100 mm. Hg; at 11 p. m. it was 94 mm. Hg. On May 5 there was no change in the respiration or radial pulse. Blood-pressure at 9 a. m. was between 95 and 100 mm. Hg; at 2 p. m. between 105 and 108; at 7 p. m. between 106 and 110.

May 6 she said she felt better. The heart action was no better, still very irregular, and the heart sounds were indistinct. The size of her heart was the same as on admission. The ice bags were continued. Morphin was given only once in the previous twenty-four hours. Respiration ranged between 24 and 30, radial pulse between 96 and 116, and apex beat between 140 and 150. At 9 a. m. the systolic blood-pressure was 105; at 3 p. m. systolic blood-pressure was 102 mm. Hg. At 5 p. m. it was 104.

On May 7 there was no change in her cardiac condition. Blood-pressure ranged throughout the day between 103 and 107 mm. Hg. There was no change in the respiration or pulse.

May 8 the systolic blood-pressure ranged between 100 and 106 mm. Hg.

May 9, it ranged between 100 and 104 mm. Hg.

May 10, it ranged between 100 and 104 mm. Hg.

There was no improvement during this period of eight days of strychnin treatment. She had received throughout this period 1/30 gr. every three hours. She was still markedly dyspneic and at times cyanotic and nauseated. The heart sounds were no clearer and the irregularity was as marked as at entrance. She was having such pains that the ice bag was kept on constantly but she had not received any morphin since May 6.

On May 10 digitalis was started, 5 mm. every four hours, continuing with the strychnin until May 18, when the strychnin was omitted and the digitalis, which had been gradually increased to 10 min. four times a day, was changed to

digipuratum, one tablet every six hours for two days, then one tablet three times a day for two days, and then one tablet twice a day. She improved somewhat on digitalis so that she was not nauseated. She had a better appetite and felt generally relieved. Her cardiac condition, except for the slowing of the rate, remained about the same as on admission. The heart was no smaller and the cardiac action was still markedly irregular. The temperature varied between 100 and 97 F.; the pulse between 60 and 80, and the respiration between 20 and 30.

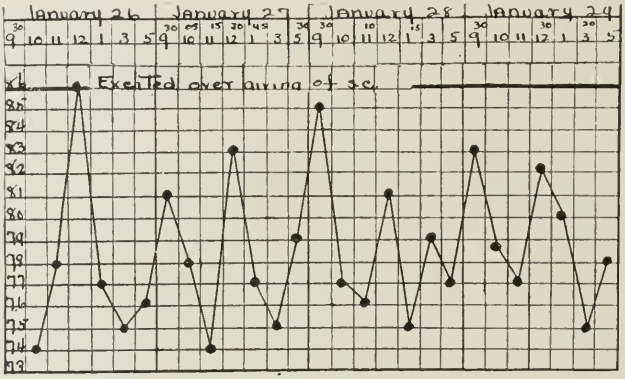

Chart 1, Case 2.—Curve showing systolic pressure in the case of M. M. under strychnin, hypodermically, at 9 a. m., 12 noon, 4 and 8 p. m. for a period of four days. Aspirin, 5 gr., every three hours (six doses in twenty-four hours) and hot baths at 7:30 a. m. and 6 p. m.

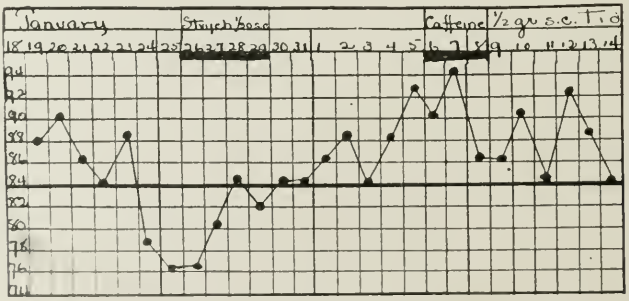

Chart 2, Case 2.—Curve showing systolic pressure in the case of M. M. under strychnin and caffein.

At this point she was taken home, against advice, to be treated by the district physician.

CASE 2.—M. M., 8 years old, hospital No. 1139; admitted January 18.

History.—Never very strong; had pneumonia, followed by measles a year before present trouble started. She had not been well since. Present illness started three weeks before admission to the hospital, with noticeable choreic movements.

Physical Examination.—A pale, emaciated child, with marked involuntary movements. Teeth were in poor condition; both tonsils were large, showing marked chronic infection. General glandular system was slightly enlarged.

Heart.—Point of maximum impulse in the fourth interspace, 8 cm. to the left of the midsternal line; left border 9 cm. to left of midsternal line in the fourth interspace, and 10 cm. in the fifth interspace. Right border 2.5 cm. to the right of the midsternal line in the second interspace. First sound at the apex was accompanied by a soft blowing murmur, which could be heard well into the axilla and back. Radial pulses were symmetrical and synchronous, small volume, low tension. With Nicholson's sphygmomanometer the systolic pressure was 80 to 90 mm. Hg. Diastolic pressure varied between 55 and 65, and continued between these limits through the patient's stay in the hospital (twenty-eight days), with the exception as noted in the charts.

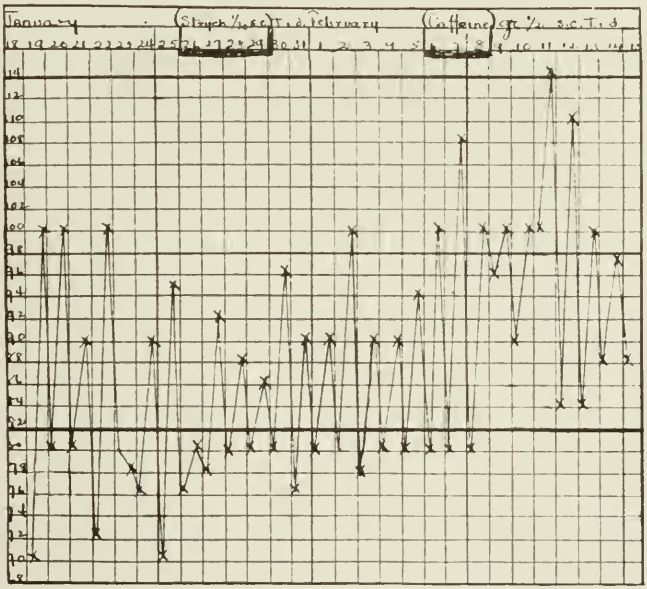

Chart 3, Case 2.—Pulse curve in the case of M. M. under strychnin and caffein.

Treatment.—The treatment consisted of 40 gr. aspirin a day for the first two days. She was given hot baths, starting at a temperature of 100 F. and gradually increasing the temperature of the water until it reached 110 to 115 F. The length of the baths ranged from half an hour to three-quarters of an hour, gentle friction being given throughout the bath.

January 26 she was put on strychnin. Her temperature from her admission until strychnin was started on January 26 ran between 98 and 99 F.; her pulse between 80 and 100, and her respirations between 20 and 30.

She received 5 gr. of aspirin every six hours — six doses in thirty-six hours. For the chorea she received hot baths at a temperature of 100 to 110 F. twice

a day, with gentle friction. She was given 1/30 gr. strychnin on January 26 at 9 a. m. The systolic pressure at that time had ranged between 80 and 100 mm. Hg. Her systolic pressure at 10 a. m. was 74 mm. Hg.; at 11 a. m. it was 78, and at 12 m. it was 86. At this time she was somewhat excited over the prospect of her second injection. At 1 o'clock p. m. the pressure had fallen to 77 mm. Hg; at 3 o'clock to 75 and at 5 o'clock to 76, one hour after her third injection of 1/30 gr. of strychnin.

On January 27 at 9:30 a. m. her pressure was 81 mm. Hg.; at 10:05 a. m. it was 78, and at 11:15 a. m. it was 74; at 12:30 a. m. it was 83, and at 1:45 p. m. it was 77. At 3 p. m. it was 75; at 5:30 it was 79.

She received 1/30 gr. at 9 a. m., 12 m., 4 and 8 p. m.

January 28 at 9:30 her systolic pressure was 85 mm. Hg. At 10 a. m. it was 77; at 11:10 a. m. it was 76, and at 12, noon, it was 81. At 1:15 p. m. it was 75. At 3 it was 79, and at 5 it was 77

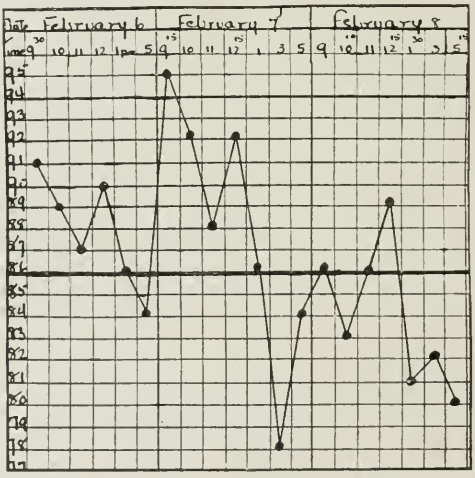

Chart 4, Case 2.—M. M., aged 8 years. Hospital No. 1139. Curves showing systolic pressure under caffein sodium benzoate, ½ gr. hypodermically at 8 a. m., 12 noon and 6 p. m. during a period of three days.

She received on this day also hypodermics at 9 a. m., 12, noon, 4 and 8 p. m.

On January 29, the last day of this series, she received 1/30 gr. of strychnin at the same hours as on the previous day.

At 9:30 a. m. her systolic pressure was 83 mm. Hg; at 10 it was 78, plus; at 11 a. m. it was 77; at 12:30 p. m. it was 82; at 1 p. m. it was 80; at 3:20 p. m. it was 75, and at 5 o'clock it was 78.

Through this period of four days, from January 26 to 29, her pulse remained constantly between 75 and 85 and her respirations between 20 and 30. She complained of no headache and there was no increase in the twitching. The urine throughout this period was normal. She then received a rest of seven days through which she received only aspirin and hot baths. She was then put on caffein sodium benzoate, ½ gr. subcutaneously, three times a day — 8 a. m., 12 noon and 6 p. m.

From January 26 to February 6 the general average of systolic pressure had risen from 84 mm. Hg to approximately 90 mm. Hg.

On February 6 at 9:30 a. m. she received her first hypodermic injection of caffein; the systolic pressure was then 91 mm. Hg. At 10 a. m. it was 89, at 11 it was 87, at 12 noon it was 90, when she received her second dose. At 1 p. m. it was 86; at 5 p. m. it was 84. The next morning at 9:15 it was 95, which was one and one-half hours after her fourth injection. At 10 it was 92; at 11 it was 88; at 12:15 p. m. it was 92; at 1 it was 86; at 3 it was 78; at 5 it was

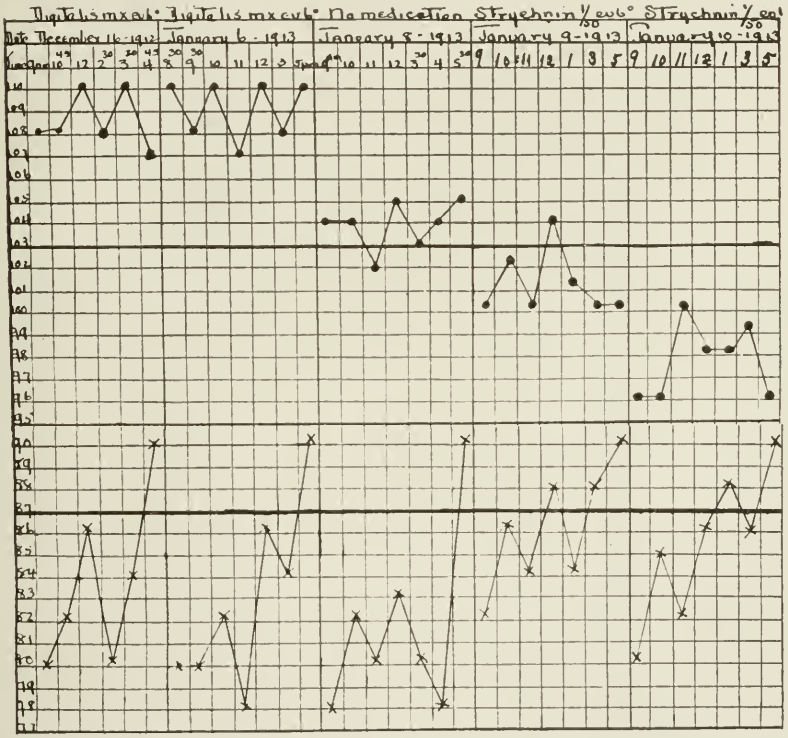

Chart 5.—M. B., aged 13 years. Hospital No. 1032. Upper curves show systolic pressure and lower curve, the pulse-rate under digitalis, under no medication, and under strychnin.

84. On February 8 she also received three injections — 8 a. m., 12 noon, and 6 p. m.

At 9 a. m., February 8, the systolic pressure was 86 mm. Hg.; at 10:10 it was 83; at 11 it was 86; at 12:15 p. m. it was 89 (fifteen minutes after her second injection for that day). At 1:30 it was 81 mm. Hg; at 3 it was 82, and at 5:15 it was 80. On the whole there was a slight decrease while on caffein. There was no increase in her choreic condition. In fact that improved steadily under hot baths. There was no increase in the pulse, which continued between 80 and

100, and her respirations continued between 20 and 30. The temperature throughout both periods of strychnin and caffein remained between 98 and 99 F.

CASE 3.—J. P., aged 10 years, hospital No. 890.

History.—The patient was always well until one and one-half years ago, when she developed rheumatic fever, with both arthritis and endocarditis. She was admitted to the hospital April 20, 1912.

Physical Examination.—The physical examination showed a well developed but poorly nourished girl; comfortable only in sitting posture; marked precordial bulging, and diffuse cardiac impulse. Right border 3 cm. from midsternal line in third interspace, and left border in midaxillary line. Palpable thrill: presystolic, diastolic and systolic murmurs; pulse irregular and small.

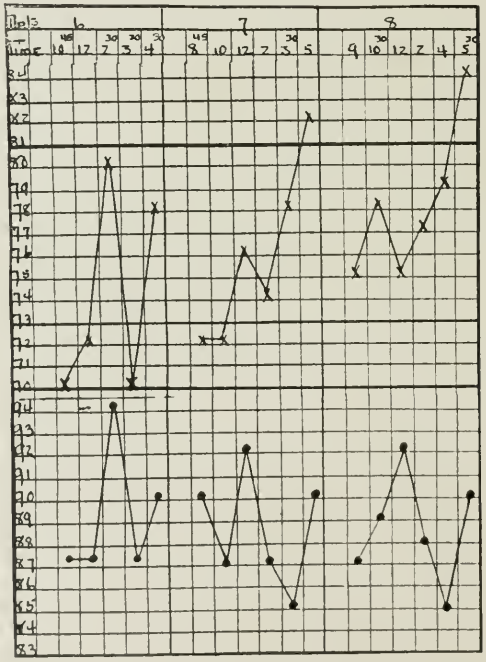

Chart 6.—M. F., aged 12 years. Hospital No. 1071. Upper curve shows pulse-rate and lower curve systolic pressure under strychnin, 1/50 gr., hypodermically, three times a day for a period of three days.

Treatment.—She was put to bed, given aspirin, 40 gr. a day, and tincture digitalis from 9 to 30 min. a day till June 10, when digitalis was discontinued. The heart had diminished in size, the left border being in the anterior axillary line; pulse had been regular and was the typical digitalis-stimulated pulse. General condition was good. She was comfortable and appetite was good.

She was given strychnin, 1/100 gr. every six hours by mouth, from June 11 to 17. By June 14 the pulse had become irregular and the heart had dilated out to the midaxillary line, but she still felt comfortable and her general con-

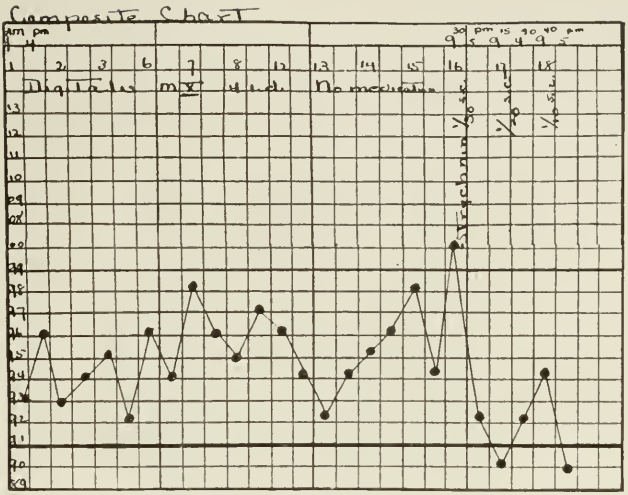

Chart 7.—J. McC., aged 13 years. Hospital No. 1138. Composite chart showing blood-pressure curve under digitalis, no medication, and under strychnin.

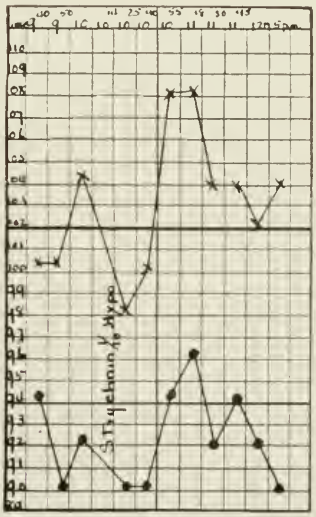

Chart 8.—J. McC. Upper curve shows pulse-rate; lower curve systolic pressure under strychnin, 1/10 gr., hypodermically.

dition remained good. By June 17, however, she was uncomfortable, pulse more rapid and she was nauseated; heart was out to the midaxillary line. She was put back on digitalis and by June 20 was feeling much better.

Effect of Strychnin: The pulse grew irregular and more rapid; blood-pressure fell; respiration at first fell, then rose; general condition not so good, nauseated, loss of appetite, precordial pain.

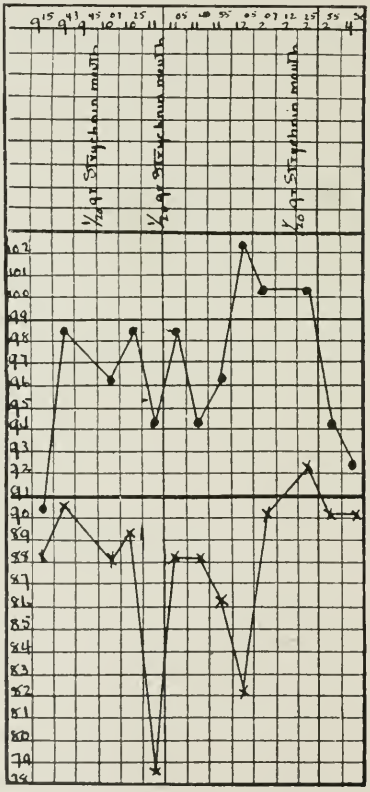

Chart 9.—J. McC. Upper curve shows systolic pressure, lower curve the pulse-rate under strychnin.

CASE 4.—M. F., aged 12, hospital No. 1071.

History.—The patient had always been a sickly child. Had measles at 3 years; jaundice at 4 years; erysipelas at 8 years. Had sore throat frequently. Was admitted to the hospital Nov. 5, 1912, with an indefinite history of pain in chest for "a long time."

Physical Examination.—The physical examination showed a fairly well developed and nourished boy, very pale and sallow. Moderate general glandular enlargement. Throat showed signs of repeated inflammation. Teeth were very poor.

Heart.—Maximum impulse seen and felt outside nipple line in fourth interspace. Left border 11.5 cm. from midsternal line in the fifth interspace, and right border 5.5 cm. from the midsternal line in the third interspace. The normal first sound was obliterated by a loud blowing murmur heard all over the precordia and transmitted to the axilla and back. There was also a murmur

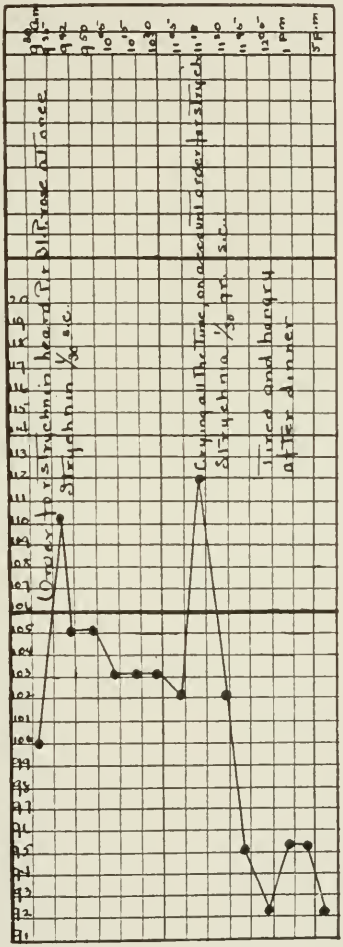

Chart 10.—J. McC. Blood-pressure curve showing the results of emotional excitement.

heard during diastole to the left of the sternum in the third and fourth interspaces. On admission his systolic blood-pressure was 90 mm. Hg, according to Nicholson's sphygmomanometer; pulse-rate 88; pulse was very soft and compressible, and not of very good quality. His peripheral circulation was poor; hands

and feet were cold, purplish, subnormal. He remained in the hospital from Nov. 6, 1912, to January 16, 1913.

Treatment.—For the first two months he was given absolute rest in bed. For the first week 25 gr. of aspirin was given in twenty-four hours; for the first three weeks digitalis 20 to 32 min. in twenty-four hours. His systolic pressure during this period remained between 85 and 95 mm. Hg. After an interval of three days without medication, on December 6 he was put on strychnin, 1/50 gr. three times a day, hypodermically, and later four times a day, which gave him from

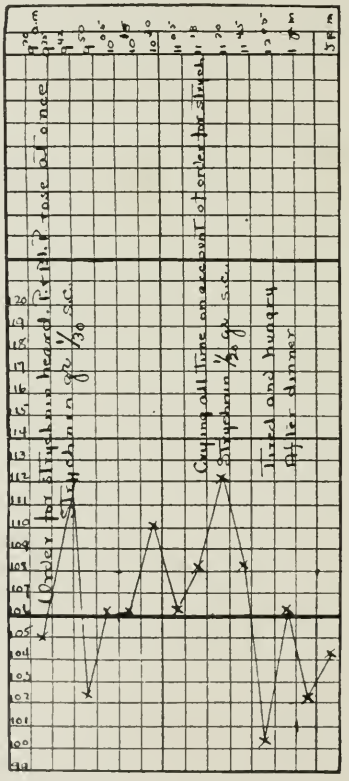

Chart 11. J. McC. Pulse curve under emotional excitement while the patient was taking strychnin.

1/12 to 1/15 of a grain in twenty-four hours. He was kept on this for three weeks. During this time his general condition improved, as would be expected from the continued rest in bed. There was no change in his pulse-rate nor in his pulse-pressure that could not be attributed to the rest in bed. His peripheral circulation improved with the improvement in his heart. The heart area had lessened by 1 cm. on the left, and 5 cm. on the right. During the next three weeks he was given no medication except a stomach tonic which contained 5 minims tincture nux vomica. During this period he was allowed up in a

wheel chair for half-hour periods twice daily. His general condition improved more rapidly than at any other period. His heart diminished in area 1.5 cm. on the left and 1 cm. on the right. Pulse and peripheral circulation improved as rapidly as at any time and he was discharged to continue treatment under careful supervision. Before going out he was put on digitalis, 5 minims, four times a day.

CASE 5.—M. B., hospital No. 1032. Aged 13 years.

History.—This child was an old heart case and had been in the hospital several times with broken compensation. She was on digitalis continuously. She had been in the hospital from Sept. 27, 1912, to the time of the present study, which was Jan. 9 and 10, 1913. She had improved so that her heart was compensating enough to allow her to be in a wheel chair for half hour twice daily. Throughout this period she had been receiving 10 min. of the tincture of digitalis every six hours. Her pulse had remained, for a month previous to the giving of the strychnin, between 80 and 100; her respiration between 20 and 30; her tem-

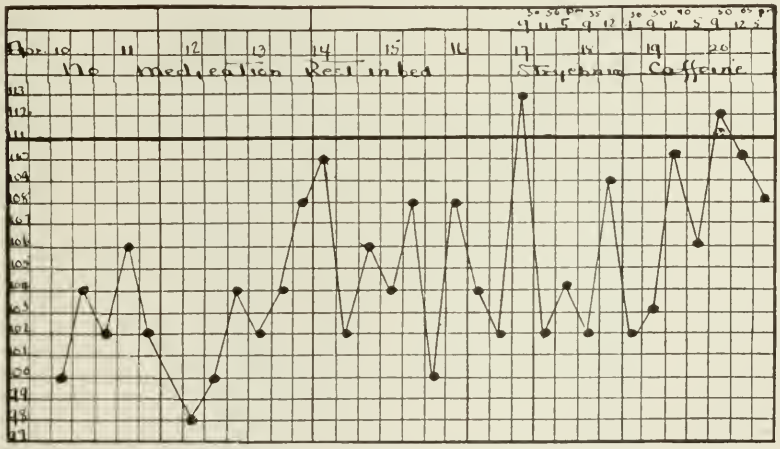

Chart 12.—L. P., aged 2 years. Hospital No. 1169. Systolic pressure curve under rest in bed, without medication, under strychnin and under caffein.

perature had been slightly subnormal, running between 97 and 98.4 F. Her general condition was good.

On the evening of January 7 all medication was stopped. Through January 8 she received no medication at all and was allowed up for her two half-hour periods. On January 9 she received 1/30 gr. of strychnin four times in the twenty-four hours starting at 9 a. m. Her systolic pressure had been running between 108 and 110 mm. Hg, while she was on digitalis. During the period of twenty-four hours when she received no medication her pressure had fallen to between 102 and 105 mm. Hg. At 9 a. m. on January 9, when she received her first hypodermic of 1/50 gr. strychnin, her systolic pressure was 100 mm. Hg. At 10 it was 102; at 11 it was 100; at 12 noon it was 104; at 1 p. m. it was 101; at 3 p. m. it was 100, and at 5 p. m. it was 100 mm. Hg.

January 10 she continued receiving every six hours 1/50 gr. strychnin, 4 doses in twenty-four hours. At 9 a. m. her systolic pressure was 96 mm. Hg; at 10

it continued at 96; at 11 it was 100; at 12 noon it was 98; at 1 p. m. it was 98; at 3 it was 99, and at 5 it was 96.

Her pulse, which while she was on digitalis had been constantly between 80 and 100, had dropped to between 75 and 80. On the whole during the two days in which she received the strychnin it remained between 80 and 90. There was no change in her temperature. She began to complain of precordial pains, from

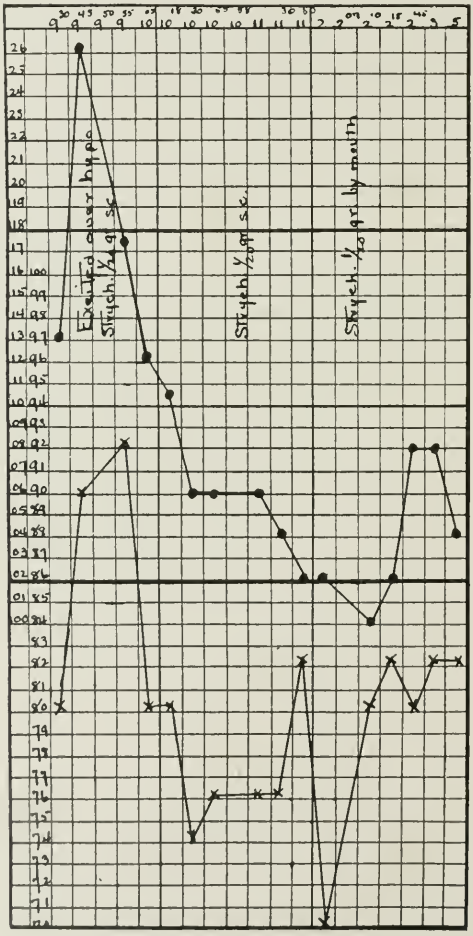

Chart 13.—L. P. Upper curve shows systolic pressure, lower curve the pulse-rate under strychnin. Both curves show a sharp rise during the excitement occasioned by the anticipation of a hypodermic injection of strychnin.

which she had been free for over a month. She was taken off of strychnin and put on digitalis, her pulse and blood-pressure returning to her normal again within forty-eight hours.

CASE 6.—J. McC., aged 15 years, hospital No. 1138; was admitted January, 1913.

History.—The patient was never a very robust boy. He had had rheumatic fever since 1909, and had had endocarditis since 1910. Had a double mitral lesion. Heart had not compensated enough for him to be able to do very much, i. e., go to school, for over a year. He was admitted to the hospital with failure of compensation, cyanotic, peripheral circulation very poor, pulse small, regular, but of very poor quality.

Heart.—Left border 12 cm. in fifth interspace, and right border 8 cm. in third interspace. On admission there was a definite presystolic thrill. The heart sounds were obscured by a presystolic and systolic murmur heard all over the precordia; second pulmonic greatly accentuated.

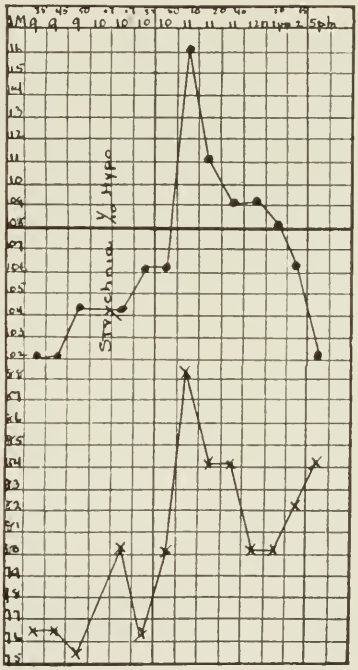

Chart 14.—L. P. Upper curve shows systolic pressure, lower curve shows pulse-rate under strychnin, 1/10 gr., hypodermically.

Treatment.—The patient was put to bed for several weeks, without any marked improvement in his general or cardiac condition, and then he was put on tincture digitalis for two months. During this period he remained in bed, except for two hot tubs daily for the peripheral circulation. He was given several courses of aspirin, 40 gr. a day, for four to seven-day periods. At this time his general condition had improved. He could sit up in a wheel chair with comfort. The peripheral circulation was very much better, and the heart area had diminished by 1 cm. on the left, and 5 cm. on the right. The pulse rate varied, ranging

between 85 and 100. Systolic blood-pressure ranged between 95 and 105 mm. Hg. Then there was a period of three days without any medication. As far as could be seen, during these three days he remained in exactly the same condition as he had been, there being no change in general condition, peripheral circulation, heart measurements, quality of heart sounds, pulse rate, or systolic blood-pressure.

His first period of strychnin treatment was begun on March 17 when he received 1/20 gr. at 9:45 a. m. At 9:15 systolic pressure was 90 mm. Hg; at 9:43 it jumped to 98, presumably from anticipation of the subcutaneous injection, as he was nervous over the preparation of his hypodermic. At 9:45 1/20 gr. strychnin was given. By 10.07, twenty minutes after the hypodermic had been given. the pressure was 96; at 10:25 it was 98. At 11 he received another

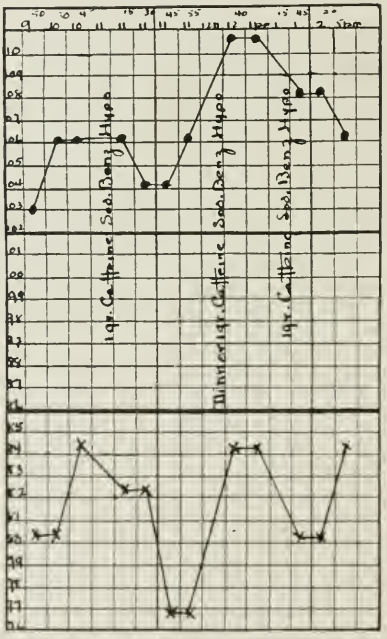

Chart 15.—L. P. Upper curve shows systolic pressure, lower, the pulse-rate under dose of 1 gr. caffein sodium benzoate hypodermically.

1/20 gr. of strychnin subcutaneously, his systolic pressure being 94 mm. Hg. At 11:05 systolic pressure was 98; at 11:40 it was 94; at 11:55 it was 96; at 12:05 noon it was 102; at 2:07 p. m. it was 100. At 2:12 he received another 1/20 gr. subcutaneously. At 2:25 it was 100 mm. Hg; at 2:55 it was 94, and at 4:30 it was 93. He was then left with no medication for almost a month, when on April 16th he was started on strychnin again.

During this interval of a month his pulse ranged between 85 and 100; blood-pressure between 95 and 105 mm. Hg. He was then allowed up and around in a wheel chair. April 16 at 9:30 a. m. his systolic pressure was 106. At 9:35 he heard the order for strychnin. The blood-pressure rose to 110. He was given the strychnin 1/30 gr. at this time and at 9:42 his blood-pressure had fallen to

105 mm. Hg. At 9:50 it was still 105; at 10:05 it was 103; at 10:15 it was 103; at 10:30 it was 103; at 11:05 it was 102. At 11:18 strychnin was again ordered and the systolic pressure rose to 112, probably because he started to cry. Strychnin was given at this time and by 11:30 his pressure had fallen to 102. He had stopped crying. At 11:45 it had dropped to 95; at 12:05 noon it had dropped to 92. At 1 p. m. it was 95 and remained so during the afternoon until 5 o'clock, when it had dropped to 92 mm. Hg. His pulse had changed with the systolic pressure throughout the day, as seen in the chart.

April 17 the dose of strychnin was increased to 1/20 gr., which he received at 9:45 a. m., 11 and 2:12 p. m. The effect of this is seen on the chart. There was a slight rise between 11 a. m. and 2 p. m. from an average of 98 to 102,

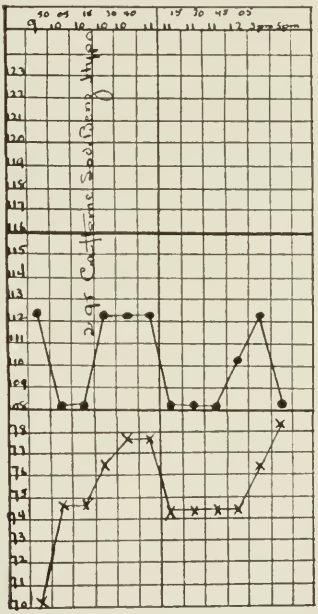

Chart 16.—L. P. Systolic pressure, upper curve, pulse-rate, lower curve, under 2 gr. dose of caffein sodium benzoate hypodermically.

remaining there until after his third injection, when it dropped back to 92 mm. Hg. There was very little effect on the pulse.

April 18 at 9:40 a. m. his systolic pressure was 94 mm. Hg; at 9:50 it was 90; at 10 it was 92. At 10:14 he received a 1/10 gr. strychnin hypodermically. At 10:25 a. m. the systolic pressure was 90 mm. Hg; at 10:40 it was 90; at 10:55 it was 94; at 11:18 it was 96; at 11:30 it was 92; at 11:45 it was 94; at 12 noon it was 92; at 5 p. m. it was 90 mm. Hg.

During these three days with varying doses of strychnin there was practically no effect, even with 1/10 gr., on his pulse or respiration. His pulse showed the greatest effect by a rise of 8 with 1/10 of a grain.

CASE 7.—L. P., aged 14 years, hospital No. 1169, was admitted March 8, 1913.

History.—The patient had chorea five years previously; otherwise had been fairly well. Her present illness had started with pain in the wrist and knees several weeks before admission.

Physical Examination.—The physical examination showed a fairly well developed, but poorly nourished girl. Slight tenderness in wrists. Temperature 100; pulse 90; respiration 20.

Heart: Left border 9.5 cm. from midsternal line in the fourth interspace, 3.5 cm. on the right in the third interspace. Sounds were not very clear, of poor

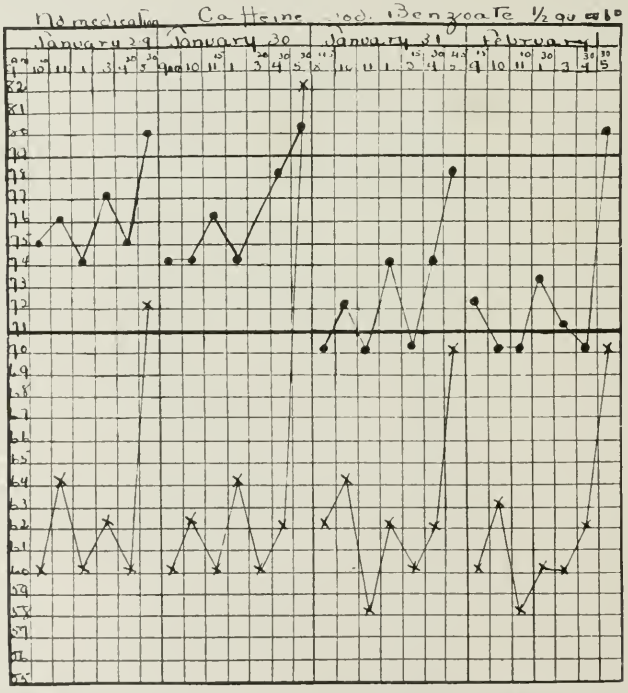

Chart 17.—A. B., aged 8 years. Hospital No. 1136. Myocarditis following pneumonia. Systolic pressure, upper curve, pulse-rate, lower curve, during period of no medication, and of caffein sodium benzoate, 1 gr.. every six hours hypodermically.

quality, but regular. There was a soft systolic murmur at the apex, transmitted to the base, the axilla and the back. Pulse was very soft, easily compressible and regular.

Treatment.—She was put to bed and given 25 gr. of aspirin a day for the first three weeks; then was given 5 gr. of aspirin three times a day. During this period she improved markedly. Her heart area diminished by 1 cm. on the left and 0.5 cm. on the right. Cardiac sounds became more clear and pulse stronger. On admission her pulse pressure had been 80 mm. Hg. At the time strychnin

was started, April 17, the systolic pressure had ranged between 100 and 110 for the last month, from almost daily observations. On the first day (April 17, see chart) of strychnin observation she was given 1/20 gr. at 9:50 a. m; at 10:50 and at 2:07 p. m. another twentieth by mouth. There was no increase in either the pulse-rate or blood-pressure and no change in her respiration. The next day she was given 1/10 gr. of strychnin sulphate subcutaneously. Within an hour there was a rise of 12 mm. Hg, with slight twitching around the mouth which lasted for an hour. During this hour her pulse remained within the usual limits and blood-pressure dropped to normal, though she still showed some slight twitching of the mouth. (See chart for April 18.) This patient was also given caffein

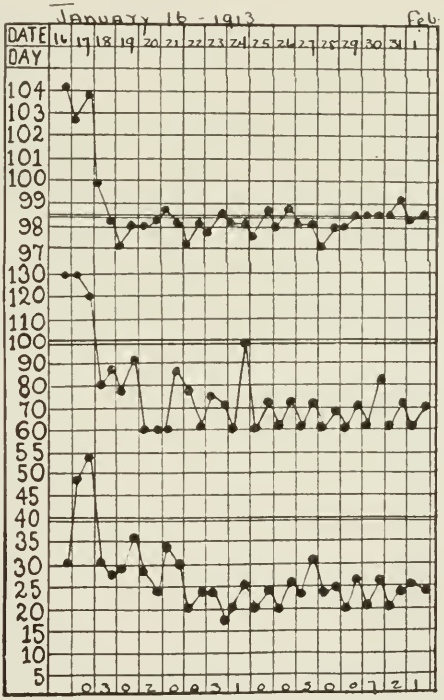

Chart 18.—A. B. Clinical Chart of course of pneumonia.

sodium benzoate. The first day, April 19, she received 1 gr. caffein sodium benzoate at 11 a. m.; another at 12 noon and a third at 1:15 p. m., making 3 grains within a period of three hours without any change in her pulse-rate or blood-pressure. The following day, April 20, she received 2 gr. in one dose without affecting either her pulse or blood-pressure. (See chart for April 19 and 20.)

CASE 8.—A. B., aged 8 years, hospital No. 1136; was admitted to the hospital January 16.

History.—The patient was a well developed and well nourished boy. He had been in good physical condition until the occurrence of pneumonia, which developed during the week of Jan. 10, 1913. He was admitted with involvement

of the left lower lobe. He developed a marked myocarditis during the crisis, which occurred in less than forty-eight hours after his admission, on January 18. He received no medication up to January 29. During this period his temperature was normal, and it remained between 97 F. and normal until January 30, when he was put on caffein sodium benzoate. His pulse had been running between 60 and 70 most of the time, very irregular and small. Respirations were between 20 and 30. During the time that he was on caffein sodium benzoate there was no change in his temperature, pulse or respiration or in his general feelings. His systolic pressure had been running between 75 and 80 mm. Hg previous to starting the caffein. January 30 he received a half grain of caffein sodium benzoate subcutaneously every six hours, starting at 9 a. m.; this was continued for three days. January 30 at 9 a. m. his systolic pressure was 74 mm. Hg; at 10 a. m. it was 74; at 11:15 it was 76; at 1 p. m. it was 74; at 4:30 p. m. it was 78, and at 5:30 it was 80 mm. Hg.

January 31 at 8:45 a. m., fifteen minutes before he received the fifth dose of caffein sodium benzoate, his systolic pressure was 70 mm. Hg; at 10, an hour after his fifth dose, it was 72; at 11 it was 70; at 1 p. m. it was 74; at 3:15 it was 70; at 4:30 it was 74, and at 5:45 it was 78 mm. Hg.

February 1 at 9:15 a. m., fifteen minutes after the ninth dose, systolic pressure was 72 mm. Hg; at 10 it was 70; at 11:10 it was 70; at 1:30 p. m. it was 73; at 3 it was 71; at 4:30 it was 70; at 5:30 it was 80 mm. Hg. With the rise in systolic pressure there was a corresponding rise in his pulse-rate. There was no change in the heart sounds, which were at all times weak, and there was no change in the irregularity or volume of his pulse as far as could be made out by digital examination.

DISCUSSION

DR. GITTINGS: I would like to ask Dr. Lucas whether the figures for the blood-pressure experiments have been based on auscultatory or palpatory methods? The auscultatory method over the brachial artery in adults, shows an 8 to 10 mm. higher systolic reading than by the ordinary palpation of the radial at the wrist. If the brachial be palpated, however, the difference does not exceed 1 to 2 mm.

DR. LUCAS: They were based entirely on palpatory methods.

CARDIAC DISEASE IN CHILDHOOD, WITH SPECIAL REFERENCE TO PROGNOSIS

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In 1906 I reported the results of an investigation of certain clinical aspects of rheumatic fever in childhood, which was based on a series of 300 consecutive patients admitted to the wards of the Children's Hospital. Of these 300 patients, 209 were discharged from the hospital with signs of organic valvular disease of the heart. The after history of these cases appeared to me to be a point of great interest, with a practical value bearing directly on the question of prognosis, and on certain aspects of treatment. I determined at the time to keep in communication as far as possible, with all of these discharged patients, and at the same time the scope of the investigation was extended beyond the limit of cardiac disease of rheumatic origin, by including all other patients of cardiac disease admitted to the hospital during the period from which the original series was taken. Cases of patients who subsequently died from intercurrent infection were thrown out.

One of the features of greatest interest in such an investigation is the amount of disability carried into adult life, or at least young adult life, by these patients. It was therefore necessary to follow the after-history of these patients for a period sufficiently long to afford evidence on this point. The period in which the cardiac patients of this series were admitted to the hospital was that of a number of years previous to the summer of 1903. I resolved to follow the cases discharged from the hospital until all of them should have entered at least young adult life, taking the age of 14 years as the termination of childhood. All of these patients have now passed this limit, the youngest survivor having reached the age of 15 years.

ETIOLOGY

The series of cases included in this investigation numbers 304 cases of cardiac disease. It throws a certain amount of light on the relative frequency of occurrence of the various etiologic factors.

TABLE 1.—ETIOLOGY IN CARDIAC DISEASE

	Cases.	Per Cent.
Rheumatic fever	264	87
Congenital lesions	21	7
Some recognized infection other than rheumatic fever	9	3
Unknown etiology	10	3

In compiling this table, in the absence of any laboratory or bacteriologic proof of the existence of rheumatic fever as a specific disease entity, the following clinical evidence of the rheumatic origin of the lesions was employed. All cases which had either during the attack in the hospital, or in previous, or in subsequent attacks, shown symptoms of arthritis or of chorea were classified as manifestations of rheumatic fever. In addition, certain cases of acute endocarditis and pericarditis with fever, in which the clinical picture was precisely similar to other cases in which arthritis did occur, and in which there was no evidence of any other form of infection, were also included. On this basis of classification, no case of acute febrile cardiac disease fell under the heading of unknown etiology, every such case being either due to rheumatic fever, or to some other recognized infection. The cases of unknown etiology were all cases of chronic endocarditis.

The table shows the overwhelming preponderance of rheumatic fever as a cause of cardiac disease.

THE CARDIAC CASES DUE TO RHEUMATIC FEVER

Acute and Chronic Cases.—Patients entering a hospital with cardiac disease, are admitted either on account of symptoms connected with the disease from which they are suffering, or the cardiac lesion is discovered accidentally in connection with the investigation of their illness. In the 264 rheumatic cases, all patients were admitted because of symptoms of this disease, either arthritic or cardiac. Arthritic symptoms in rheumatic fever, under the present most generally accepted theories of the etiology of this disease, may always be regarded as evidence of the existence at the time, of an active infection. Cardiac symptoms, on the other hand, may occur from two causes. They may be due to the existence at the time of an active infection localized in the heart, or they may be due to the so-called broken compensation, caused by calling on a damaged heart to perform a work which is too great for its power. All the cases in the series which had, during their stay in the hospital, symptoms of arthritis, or in which the cardiac symptoms were accompanied by the regular febrile course characteristic of an acute infection, are classified

as acute infections. Those cases in which the cardiac symptoms were unaccompanied by fever, and in which there was no history of an immediately preceding febrile attack, are classified as chronic endocarditis.

The relative proportions of acute and chronic cases in the series are shown in Table 2.

TABLE 2.—PROPORTION OF ACUTE AND CHRONIC CASES

	Cases.	Per Cent.
Acute Infection	206	78
Chronic endocarditis	58	22

It appears, therefore, that in childhood, the causes which lead a patient to seek hospital treatment, are more often the symptoms produced by the acute infection with rheumatic fever, than those produced by its after-effects on the heart.

Relation of Cardiac Symptoms to Infection.—In my former paper I expressed the view that in childhood, as distinguished from adult life, cardiac symptoms are more often due to an actual present infection localized in the heart, than to the overstraining of a permanently damaged heart. I believe that the converse of this view is also true. In adult life, the development of an acute endocarditis in the course of an attack of rheumatic fever, is usually described as an insidious process, manifesting itself by the development of an endocardial murmur. In childhood the occurrence of an acute endocarditis is usually accompanied by actual symptoms referable to the heart. The set of symptoms called cardiac, such as precordial pain, palpitation, cough, dyspnea, orthopnea and eventually enlarged liver and edema, are in adults almost always attributed to overstrain. In childhood, this train of cardiac symptoms undoubtedly may be due to this cause, but in the majority of cases it is due to the existence of an actual present cardiac infection. Of course the symptoms are due to an inability of the heart properly to perform its work, but the cause of this inability is to be found in a fresh cardiac infection. The incompetence of the heart is not dependent on the actual amount of valvular insufficiency or stenosis present, for it bears little or no relation to the lesion. It is probably due to the acute myocarditis, which is known to be a frequent, if not an almost invariable, accompaniment of acute rheumatic endocarditis. The accompanying tables give evidence of the relation of cardiac symptoms to the presence of an actual infection:

TABLE 3.—CASES ADMITTED FOR CARDIAC SYMPTOMS

	Cases
Acute infection present	100
Acute infection absent	37

This consideration is of interest in reference both to prognosis and treatment, for it is recognized that the cause of death in the majority of these cases is cardiac failure. If the symptoms leading to such failure are most frequently due to infection, or reinfection, and not to overstrain, this fact has an obvious practical bearing.

In any event I wish to deprecate the use of the term broken compensation as applied to the train of cardiac symptoms described under this name when they occur in childhood. Apparently in only a relatively small number of cases is this term, and the theory on which it is based, applicable to the clinical picture as seen in childhood. In the majority of cases, the cause is not overexertion, but fresh infection. The term cardiac insufficiency is far preferable to broken compensation, as it is equally applicable to both causes.

The Cardiac Lesions.—The relative frequency of occurrence of the various cardiac lesions is of interest in connection with the subsequent history of these cases. The relation of the form of lesion to prognosis is still a more or less unsettled question in the cardiac disease of childhood. The cases, classified on the basis of the lesions shown during their stay in the hospital, were as shown in Table 4. In only two cases was pericarditis found without any evidence of a valvular lesion in addition. The fifty-eight cases of pericarditis are classified both as pericarditis and according to the endocardial lesion present, and fifty-six of them are counted twice.

TABLE 4.—OCCURRENCE OF THE VARIOUS CARDIAC LESIONS

	Cases
Mitral insufficiency alone	165
Mitral stenosis alone	5
Aortic insufficiency alone	1
Mitral insufficiency and stenosis	79
Mitral and aortic insufficiency	8
Mitral insufficiency and stenosis with aortic insufficiency	4
Pericarditis	58

Liability in Childhood to Recurrent Attacks of Rheumatic Fever.—The liability in any child attacked by rheumatic fever to recurrent attacks is probably the most important factor in all considerations of the prognosis of the disease. In my first paper the liability to recurrence

could only be judged on the basis of the history of attacks of rheumatic fever previous to the one under treatment in the hospital. At present, additional evidence is available, from the following of the subsequent history of the patients throughout the remainder of their childhood, and into adult life, through a period of at least nine and one-half years.

TABLE 5.—SHOWING PROPORTION OF RECURRENCES

	Cases
Died in the first attack	17
Recovered without recurrence	47
Recurrent attacks	200

It will be seen that more than one attack of the rheumatic fever infection occurred in 76 per cent. of the cases. Only 17 per cent. showed no recurrence, as in the remaining 7 per cent. no conclusions could be drawn.

Mortality.—The complete investigation of this series of cases seems to me to be of considerable value in connection with the question of the mortality in children with hearts attacked by the rheumatic fever infection. The mortality of the cases in the hospital affords a basis for estimating the liability to death in any one attack of the disease. This is shown in Table 6.

TABLE 6.—IMMEDIATE MORTALITY OF RHEUMATIC CARDIAC DISEASE

	Cases
Died in hospital	55
Discharged, relieved	209

This gives an immediate mortality of 20 per cent. The immediate mortality apparently varies with the character of the process present, as shown in Table 7.

TABLE 7.—IMMEDIATE MORTALITY IN RELATION TO THE CARDIAC LESION

Acute endocarditis	27	out of 148	cases or 12 per cent.
Acute pericarditis*	18	out of 58	cases or 31 per cent.
Chronic endocarditis	10	out of 58	cases or 17 per cent.

* In all but two of these cases acute endocarditis was probably also present.

Table 7 also shows how much more frequently death occurs as a result of an acute infection with rheumatic fever, than as a result of the overstraining of a chronically damaged heart. In forty-five of the fifty-five fatal cases the patient died in the course of an attack of acute infection, so that the mortality from this cause is 82 per cent. of the total.

The subsequent mortality of the cases in this series represents the chances against a child who has recovered from the attack of rheumatic

fever in which he is first seen, but who is left with an organic cardiac lesion. The figures are shown in Table 8.

TABLE 8.—SUBSEQUENT MORTALITY OF RHEUMATIC CARDIAC CASES DISCHARGED FROM THE HOSPITAL

	Cases
Lost to view	29
Alive	88
Dead	92

This gives a subsequent mortality of at least 23 per cent. of all cases, and if, as is fairer, the cases lost to view are thrown out, the mortality of these cases is 51 per cent.

The final mortality is that of all cases whether death occurred in the original investigation or after the discharge of the patient from the hospital. It represents the general mortality of rheumatic cardiac disease for ten years, and the chances, so to speak, in the next ten years, against any child attacked by rheumatic fever with cardiac involvement. It is shown in Table 9.

TABLE 9.—FINAL MORTALITY OF RHEUMATIC CARDIAC DISEASE

Died	147
Lived	88

This gives the final mortality as 63 per cent. This of course represents, not the mortality of rheumatic fever, but only of the cases of rheumatic fever in which the heart is affected. During the period from which the figures of this paper were taken, only 17 patients with rheumatic fever were discharged from the hospital without evidence of a cardiac lesion. Of these 17 patients, 5 remained well, 5 were lost to view, and 7 had recurrence of acute infection with cardiac involvement. Of these latter, 3 died. Including the 12 cases of rheumatic fever which could be followed, the final mortality of rheumatic fever in childhood is 60 per cent.

Relation of Mortality to Age and to Acute Infection.—This relation is one of the most interesting results of the present investigation. The basis on which the conclusions are drawn is shown in Table 10.

TABLE 10.—RELATION OF MORTALITY TO AGE AND TO ACUTE INFECTION

	Total	Acute	Chronic
Died before 14 years	140	109	31
Died after 14 years	7	1	6

In this table the cases placed under acute are those in which the patient died in an acute febrile attack, while those placed under chronic

died from cardiac failure apparently following the weakening of the heart from overstrain. It appears from the table that a great majority of the patients died as the result of an attack of rheumatic fever, and not as a result of chronic endocarditis. Even among the ninety-two patients who died after their discharge from the hospital, the majority, sixty-five, died in, or shortly after, an acute febrile attack. Such an attack was the cause of the cardiac symptoms producing death. Therefore not only the figures showing the immediate, but also those showing the final, mortality of rheumatic cardiac disease, point to infection as the chief cause of death.

But when the age at which death occurred is considered, the results are of still greater interest. The average age of all the patients at the time of the original investigation was 9 years. Therefore, ten years having elapsed since, at least an equal amount of childhood and young adult life has been lived by these patients. As more than ten years have elapsed since the majority of the original records were taken, more years have been spent over than under 14 years. Nevertheless, the table shows that the great majority of the patients in which a fatal ending occurred, died while still in childhood. Of the ninety-five patients who passed their fourteenth year, only seven have died, while 140 patients died in childhood. These results surely suggest that rheumatic fever is a vastly more serious and fatal disease in childhood.

The significance of the particular valvular lesions present during the patients' stay in the hospital in connection with the mortality of rheumatic cardiac disease does not appear to be great. The study of the valvular lesions in the fatal cases is not conclusive, because of the great preponderance of mitral insufficiency. The only result which is at all suggestive, is that no patient in whom the aortic valve was affected is now alive.

I believe there are three causes of the very great mortality of rheumatic fever in childhood. First, the greater liability of children to be attacked with rheumatic fever; second, the greater liability of children to recurrence; third, the greater liability of children to cardiac involvement. I cannot give figures in support of all these statements, but the facts are well known to most pediatrists. Table 10 shows that only one patient died after 14 years of age as the result of recurrent acute infection, the other six dying from chronic endocarditis. But 109 patients died under 14 years of age as the result of an acute infection.

We can only conclude that the chief danger in children with rheumatic cardiac disease is in childhood. The danger of death even from chronic endocarditis is greater, as thirty-one out of 140 patients died of chronic endocarditis in childhood, whereas six out of ninety-five patients died from this cause in young adult life. The chief cause of the danger during childhood, however, is the liability of children to recurrent attacks, in which an acute infectious process localized in the heart is the cause of the cardiac insufficiency leading to a fatal ending.

The Disability Following Rheumatic Cardiac Disease Acquired in Childhood.—This is a question of the greatest importance. The survival of eighty-eight patients now under observation, all of whom have entered young adult life, gives a basis for conclusion. The amount of disability is shown in Table 11.

TABLE 11.—DISABILITY IN CARDIAC DISEASE ACQUIRED IN CHILDHOOD OBSERVED IN YOUNG ADULT LIFE

	Cases
Disability great	2
Disability slight	9
Disability none	77

The patients with great disability are unable to work or to lead normal lives. Both of them have been in an adult hospital with broken cardiac compensation. Cardiac symptoms are brought on by comparatively slight exertion. The patients with slight disability have dyspnea on exertion, and some have occasional cough and slight edema. None of them has had an attack of severe broken compensation. They are able to work at sedentary occupations. Seventy-seven patients have no disability. Most of them work, and all of them are apparently leading perfectly normal lives, having had no cardiac symptoms since their childhood. My last set of reports contain many references to activity in dancing on the part of the girls, and in basketball and baseball on the part of the boys. One of the latter asked my permission to enter the twenty-five-mile marathon race. All of these eighty-eight patients still had their cardiac murmurs when I last saw them. The relation of the amount of disability to the particular valvular lesion is shown in Table 12.

TABLE 12.—RELATION OF DISABILITY TO THE VALVULAR LESION

Great disability	2	patients have mitral insufficiency
Slight disability	8	patients have mitral insufficiency
	1	patient has mitral insufficiency and stenosis
No disability	56	patients have mitral insufficiency
	19	patients have mitral insufficiency and stenosis
	2	patients have mitral stenosis

When the relative occurrence of the various lesions is taken into account, this table shows no relation between the amount of disability and the character of the valvular deformity.

The relation of the amount of disability to the age at which the patient had his first attack of rheumatic fever is shown in Table 13.

TABLE 13.—RELATION OF DISABILITY TO AGE OF FIRST RHEUMATIC ATTACK

Disability	Age in First Attack, Years	Number of Cases
Great	12 and 13	2
Slight	10 to 14	9
None	2 to 6	50
	6 to 10	20
	10 to 14	7

This table shows that all the patients with disability were attacked when past the age of 10 years, whereas in the cases without disability, the majority were first attacked in early childhood. It suggests that the earlier in childhood a cardiac lesion is acquired, the better will be the result as regards the ability to lead a normal adult life.

It seems to me that the general amount of disability seen in rheumatic cardiac disease acquired in childhood is remarkably small. I believe it to be very much less than the disability following rheumatic endocarditis acquired in adult life. Unfortunately, I cannot give figures bearing on this point, as, while rheumatic fever is fairly common in adults, it attacks the joints alone with such greater frequency than in childhood, that cases in which endocarditis develops for the first time in adult life are comparatively rare. I have not had time to accumulate a sufficient number of such cases to afford a basis for comparison. I believe, however, that such a comparison would show a much less disability in cardiac disease acquired in childhood. My recollection of my work in an adult out-patient department, and in a general hospital, is that the majority of patients suffering from broken compensation or serious disability from chronic endocarditis, could trace the origin of their lesion, if at all, to some attack of rheumatic fever occurring since they had entered adult life. On the other hand, in every adult out-patient department are seen many patients who are seeking medical aid on account of some affection other than cardiac, in whom, in the course of routine examination, some valvular lesion of the heart is found. In a large number of cases these patients declare that they have never suffered from cardiac symptoms, and have no recollection of any attack of rheumatic fever. I believe that in very many of such patients, the

cardiac lesion represents the sequela of an attack of rheumatic fever which occurred in childhood, at an age when the arthritic manifestations are often or so much less pronounced, that they are not remembered. These patients, leading normal lives, yet with every evidence of organic cardiac disease, are common. They correspond to the seventy-seven cases in my series in which no cardiac disability persisted.

A possible explanation of this lessened disability in cardiac disease acquired in childhood, is suggested by the inferences from Table 13. The disability appears to be less, the earlier in childhood the lesion is acquired. In many of the permanent lesions acquired in childhood, the power of adaptation between the damaged organ and the work required of it is greater, and children show a marvelous power of adapting themselves to the requirements of life. In the case of cardiac disease, I believe the so-called compensation of the damaged heart is more than a mere mechanical hypertrophy. I believe that when the lesion occurs during childhood, that is, during the period of active growth, a mutual adaptation between the heart and the child gradually occurs, which is far more perfect than can occur after the period of growth is passed. The child grows up to fit its heart, and the heart develops to fit the child. Only in this way can I explain the facts suggested by this paper. The earlier in life the damage to the heart, the longer is the period of growth during which this adaptation can occur.

Inferences as to the Treatment of Cardiac Disease of Rheumatic Origin.—The outcome of the patients discharged from the hospital is suggestive as regards treatment. Treatment in the chronic endocarditis of childhood resolves itself largely into the question of prophylaxis. If the sole danger to be apprehended were the rupture of compensation by overstrain, prophylaxis would consist simply in the guarding of children with damaged heart valves from overexertion. But we have seen that the chief danger lies in the liability to a recurrent attack of the infection. We know so little of the exact nature of the infecting organism in rheumatic fever, and of its channels of invasion, that we can accomplish comparatively little in preventing recurrent attacks, beside the most general hygiene measures. The evidence in favor of the tonsil as a frequent route of invasion is so great, that, in view of the fatality of the disease, I believe we are justified in advocating the removal of the tonsils in every patient who has had one attack. If a patient who, in addition to having had an attack of rheumatic fever, is subject to tonsillitis, removal

of the tonsils is positively indicated. The frequency and severity of rheumatic fever appears to vary somewhat with climate and locality. Whenever it is possible, I believe we should lessen the chances of reinfection by removing the patients to a place where rheumatic fever is uncommon.

The most important question is how far we should go in guarding against the breaking down of cardiac compensation by overstrain and overexertion. That children are liable to danger from this cause is a fact, as shown by the thirty-one patients in this series who died from chronic endocarditis while still within the limit of childhood. That we should endeavor to guard against dangerous overstrain goes without question. But it is questionable how far our efforts should reach in limiting the normal activities of the child. We must consider the question of lessening the disability in adult life, when the heart must be able successfully to cope with the strain of a normal active life. If such ability is due to a gradual adaptation between the child and the heart, it is very probable that too much limitation of the activities of childhood will prevent this adaptation from taking place, and will leave the child unfitted to encounter the demands of active adult life.

Most of the parents of the patients in my series were given strict directions as to the guarding of their children from overstrain, and as to the limiting of their activities. Some of them followed these directions, while the majority disregarded them entirely. Singularly enough, of those who obeyed these directions at all, the majority obeyed them with exaggeration, limiting the activities of the children to an extreme degree. The relation of the limitation of activity to the mortality from chronic endocarditis is shown in Table 14.

TABLE 14.—RELATION OF TREATMENT TO MORTALITY

	Carefully Guarded	Normal Activity
Died, 37	13	24
Lived, 88	20	68

The proportion of children who lead a life of normal activity during childhood is greater in those who lived than in those who died. It does not seem from this series at least as if the guarding of children from overexertion had any notable effect on the mortality. Moreover, when the cases are analyzed as to the relation between limitation of activity and subsequent disability, it appears that in general those children did better in whom the normal activities of childhood were not limited at all.

I do not mean that we should let our cardiac patients engage in all normal activities without limit, or without supervision. I simply wish to point out the possibility of going too far toward the other extreme. I believe we should avoid putting our cardiac patients under a glass case, for even normal activity is preferable to extreme limitation of activity. We should remember the other aspect of the question, that of the gradual adaptation of the child to the damaged heart, which takes place during the previous period of growth. We must do all in our power to favor this process, and this can only be done by allowing the heart to accustom itself to increasing demands on its power during this period. Nothing can be more important than the proper management of these cases, for I believe that the future of the child is largely dependent on it. The most thorough supervision is essential. Beginning at an early period after the disappearance of symptoms, with passive motion against increasing resistance, we should constantly increase the amount of activity allowed, by regulated exercises, so long as we can keep within the danger limit, of which the warning signs are extreme rapidity of cardiac action, or slight dyspnea. But we should not stop when a moderate amount of activity can be indulged in without symptoms. We should continue to increase the amount of activity allowed, and if finally these children can indulge in all the activities of childhood without symptoms, I believe we should not hesitate to remove all limitations. Their chief danger during childhood lies in reinfection, not in overexertion, and the more they learn to do in childhood, the better are their prospects for a normal, active, useful adult life.

CONGENITAL CARDIAC DISEASE

The cases of congenital cardiac disease in this series are too few to permit the drawing of conclusions of any great value. There were twenty-one cases.

Open Ductus Arteriosus.—Fifteen cases were diagnosed as open ductus arteriosus. The patients had a murmur, but no enlargement of the cardiac dulness. Two of them had slight cyanosis but no thrill, and two had a palpable thrill but no cyanosis.

The final result in these cases was as follows: Two died, four were lost sight of and nine recovered. The two patients who died, were those having slight cyanosis, and who died in infancy. In one the diagnosis was confirmed at autopsy. Both of the cases in which there was a palpable thrill recovered, with disappearance of the thrill. In all of the

nine cases of recovery, and in two of the patients lost sight of, the murmur eventually disappeared, but I am unable to state the exact time of its disappearance. The nine patients are now apparently well, and are between 10 and 16 years of age.

Pulmonary Stenosis.—Five cases were diagnosed as pulmonary stenosis. The patients had a murmur, cyanosis, palpable systolic thrill and enlargement of the area of cardiac dulness. Of these cases, four patients died before they were 2 years old, and one recovered. This patient is still very cyanotic, with the same signs and clubbed finger tips.

Deficient Ventricular Septum.—In one case this diagnosis was made. There was a murmur, enlargement of the cardiac dulness, no cyanosis and no thrill. This patient, seen at 8 months, lived a year, and was then lost sight of.

It would seem that open ductus arteriosus is a comparatively favorable lesion. The most interesting feature is the disappearance of the murmur in the patients who recovered. As open ductus arteriosus is due to a failure of the closing of the ductus by normal obliterating endarteritis, I believe the disappearance of the murmur suggests that the closure is simply delayed, and may normally occur later. In these cases, without thrill, cyanosis, or enlargement, I believe that as far as the cardiac lesion is concerned, a most favorable prognosis should be given.

ENDOCARDITIS OF OTHER ORIGIN THAN RHEUMATIC FEVER

Beside the congenital cases, there were only nineteen cases of endocarditis in the series which could not be connected with the rheumatic fever infection. Of these, ten cases were of unknown origin. Rheumatic fever could not be excluded, but no connection with this infection was found either in their past or subsequent history. Of these cases, four patients were lost sight of, three entered adult life with signs of mitral insufficiency, but no disability, and in the remaining three the murmur disappeared and they are well.

Of the nine remaining patients, two were fatal cases of purulent pericarditis following pneumonia, and two were fatal cases of malignant endocarditis following an alveolar abscess and mastoiditis, respectively. In the other five cases the cardiac lesion was attributed to scarlet fever. Two of the patients were lost sight of and three have no disability. In one of these the murmur has disappeared.

CONCLUSIONS

1. Rheumatic fever is very much the commonest cause of cardiac disease in childhood.

2. Cases with acute rheumatic infection localized in the heart are much commoner than cases suffering from chronic endocarditis.

3. Cardiac symptoms are due to two causes: first, acute infection localized in the heart; second, broken cardiac compensation. Of these two causes the first is the commoner.

4. The liability of children to recurrent attacks of acute rheumatic infection, in any of which the heart may be involved, is very great.

5. The immediate mortality of rheumatic cardiac disease is about 20 per cent.

6. The subsequent mortality of patients with endocarditis of rheumatic origin, followed for at least ten years in about 50 per cent.

7. The final mortality of rheumatic fever followed for at least ten years is 60 per cent.

8. The mortality is seen chiefly during childhood. The mortality after young adult life is reached falls to only 7 per cent.

9. The cause of death is heart failure. The cause of the heart failure may be either acute cardiac infection or broken compensation. In childhood the former cause is far the more common. After adult life is reached the latter cause is more common.

10. The particular valvular lesion present has little or no relation either to the mortality or the amount of disability in adult life; except that aortic disease appears to be a particularly fatal lesion in childhood.

11. The causes of the great mortality of rheumatic fever in children are, first, their greater liability to this infection; second, their greater liability to recurrent attacks; third, their greater liability to cardiac involvement.

12. Patients who escape the dangers of childhood, and who enter adult life, are apt to show a remarkable freedom from disability. The majority of such patients can lead normal active lives.

13. The probable cause of this freedom from disability lies in the fact that the cardiac damage occurs during the period of growth, and during this period a particularly perfect adaptation can take place between the heart and the patient, which enables the heart to meet the demands made on it. This adaptation is more perfect than can be attained in the adult.

14. The earlier in life the cardiac lesion is acquired, the better is apt to be the result in adult life, as concerns ability to lead an active, normal existence; provided that the patient escapes the dangers of childhood.

15. Treatment should be directed toward favoring the adaptation of child and heart. While guarding against overstrain, we must avoid too great limiting of the normal activities of childhood.

16. In congenital cardiac disease, open ductus arteriosus is a favorable lesion.

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DISCUSSION

DR. NORTHRUP: At the New York Foundling Hospital, where the ages of the children range from birth to 3 years, we have done autopsies aggregating in round numbers 2,000 cases, and including the work of Dr. Nicoll, the number of autopsies will reach perhaps 4,000. There were no cases of acute endocarditis except one and that seemed to be connected with general bacteremia. It was what we are accustomed to call ulcerative malignant endocarditis.

With regard to the question of recurrences, no matter how bad it may be on the first attack there is hope that it may recover, the prognosis in children is so good. Young hearts are strong and children can stand a great deal. I showed in clinic some time ago a doctor's son with rheumatic endocarditis. The attack had been so severe and so comprehensive that it might have been called pancarditis, and yet the child entirely recovered. He got so well that when his mother brought him to my house some months afterwards I did not find anything the matter with his heart. I presented him to the clinic as an athlete, a swimmer and a long distance runner, and he was as fine a specimen of young manhood as ever I have seen.

As to the general prognosis, I have found that however much of a cardiac murmur a child has, it is wise to say that the child will probably get over it within a few years. Many a doctor has brought his child to me sick at heart because of "murmurs," and has gone away encouraged, because I gave him this prognosis. I have besides made many friends from this hopefulness. I think the prognosis is good on the first attack of endocarditis in a child, however bad the case, but second attacks or chronic cases are quite another question.

DR. LA FÉTRA: I agree with Dr. Northrup that during the early years of childhood the prognosis is very much better. In children from 2 to 7 years of age the cases are more easily controlled, for it is feasible to keep them in bed from ten to twenty weeks, if necessary. Older children are more difficult to manage and it is more difficult to secure the coöperation of the parents to keep them in bed for the necessary three to six months. When the heart is attacked the thing to do is to give it rest and the chance to recover. I agree also in regard to the mortality of these cases. Aside from aortic lesions it makes little difference what the lesions are, the whole of the heart is likely to be attacked and there may be several lesions combined; also frequent attacks are the cause of fatal terminations. I am sorry Dr. Dunn did not include the second attacks from tonsillitis. I have found if we can get the tonsils in good condition the danger of the second attack is very much less. Recently I have been particularly interested in this subject and have found that a number of children with

cardiac recurrences are victims of diseased tonsils and subject to tonsillitis. In most of these cases the tonsils ought to be removed as a prophylactic measure.

DR. HEIMAN: I believe we all have come to regard tonsillitis as one of the causes of acute endocarditis. Rheumatic fever, chorea and tonsillitis are three diseases that we know belong to the sensitizing class. We also know that the primary manifestation of rheumatic fever may appear as an acute rheumatic endocarditis. In regard to relapses, I believe they are in reality reinfections.

DR. MCCLANAHAN: I merely wish to ask one question that has not come out in general discussion here, and that is, just what is the influence of cardiac conditions on the bodily growth and weight throughout childhood? Secondly, are these hearts larger than the normal heart? That is, the hearts of the cases that have apparently recovered. Is the area of cardiac dulness greater than in the normal heart?

DR. DUNN: Dr. Northrup spoke of cases under 3 years of age. The average age of these children I have reported was 9 years of age. Fifty-five died out of 200 consecutive cases. There were fifty-eight cases of pericarditis and the mortality was 31 per cent. In those cases of the series due to other causes such as scarlet fever, etc., the murmur disappeared, but in the rheumatic cases it had not disappeared and the area of dulness persisted. I think the point of Dr. La Fétra's question is well taken. I always look after the tonsils of children having had tonsillitis, especially after the first attack. I omitted this point from my paper but I advocate the removal of the tonsils after the first attack of endocarditis.

STUDIES ON THE INCUBATION PERIOD. NO. 1—SERUM DISEASE *

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By way of review it may be said the knowledge that has come to us through the biochemic reactions which take place when horse-serum is injected into the body has compelled us materially to alter our conception of the incubation period. Formerly we contented ourselves with the belief that the time which elapses after the pathogenic substance enters the body until the development of the first symptoms of the disease is the incubation period. By this we meant that the causal agent entered and grew in the body until it had reached a sufficient amount to bring about disease symptoms; in other words, that the invading army increased in size from day to day until it was able to overcome the natural resisting forces of the body. We now know that certain substances, such as horse-serum and egg albumin, when injected into the body require a certain length of time to elapse before any noticeable effects are seen or felt by the patient.

In the early days of diphtheria antitoxin and of serum therapy in general, much inconvenience was experienced by individuals injected because of the occurrence of urticaria, joint swelling, edema, glandular enlargement, etc., in an appreciable percentage of the cases. It was soon found, however, that these manifestations were due to the horse-serum itself and in no way to the diphtheria antibodies it contained. It was further found that if the antibodies were carried in a smaller quantity of horse-serum these unpleasant symptoms did not occur with the same regularity. It was also observed that an indefinite time usually elapsed after the injection of the serum before the development of the symptoms. At first little attention was given to this and it remained for Arthus and particularly von Pirquet and Schick to see an explanation for it.

Prior to the work of Arthus and von Pirquet and Schick, knowledge had accumulated concerning hypersusceptibility. It had been demon-

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strated that foreign proteid substances (cells, blood-serum, milk, tentacles of actiniae, egg albumin[1]) injected into the body sensitized the organism ("disturbed Chemismus") to the proteid, and that after a certain number of days had passed, the body for a period of time, sometimes longer than others, was sensitized in such a way that should it ever receive a second injection certain definite and typical manifestations would show themselves.

On June 16, 1903, Arthus communicated to the *Societe de Biologie*, Paris, the result of researches he had made on the effect of repeated injections of horse-serum in the rabbit (intraperitoneal, intravenous, subcutaneous). He observed in rabbits, which received repeated injections of horse-serum on successive days, that after the third injection the resorption was accomplished only after several hours. After the fourth to the seventh injection definite marked phenomena occurred in the skin over the point of injection; redness, swelling, edema, and finally necrosis with prolonged healing. He determined that these phenomena were not due to a local change in that particular area of the skin, but were dependent on two factors, namely, a primary injection, and a second injection preceded by a time interval during which a general reaction of the body had taken place, rendering it hypersusceptible or anaphylactic.

Von Pirquet and Schick, working independently (June 25 and November, 1903), from an entirely different viewpoint, that of clinical medicine, saw in the experience encountered with the use of diphtheria antitoxin and Moser's scarlet-fever serum, a typical anaphylactic reaction. Most of the symptom-complex of serum-disease had been known to the earlier observers, but, as von Pirquet and Schick remark, "they arrived at no composite picture, because they did not recognize the [irregularity] of the incubation period which occurs between the injection and the appearance of the clinical symptoms." Von Pirquet and Schick observed that when the cutaneous manifestations showed themselves early, within one to three days, they did so only in individuals who had at some previous time received an injection of horse-serum. In the fall of 1902 von Pirquet made an observation which gave him the key to a new conception of the incubation period. "A child had been injected with 10 c.c. Moser's scarlet-fever serum. After an incubation of seven days the serum symptoms appeared and lasted several weeks. After the disease symptoms had entirely disappeared—fifty days after the first injection—the

1. Metchnikof, Richet.

child, on account of a diphtheria case in the same room, was injected with 2 c.c. of antidiphtheria serum (a quantity which in a person injected for the first time never produces symptoms). Fifteen minutes later the boy began to cry and showed signs of vomiting. At the same time edema of the lower lip appeared and rapidly spread to the entire face. In a few hours there was generalized urticaria. Therefore, after the first injection the incubation was seven days, after the second injection the reaction followed at once." To this condition von Pirquet and Schick gave the name serum disease, the symptoms of which are as typical as those of the exanthematous diseases. The question very soon naturally arose, Why does not every person who receives an injection of horse-serum show the symptoms of the disease? The answer to this question was to be found in the early experience with diphtheria antitoxin; that is, it is in the first instance a quantitative affair. A very large dose produces symptoms, a small one does not. However, a still further observation is frequently made. In one person a large dose may cause visible symptoms, while in another person of equal weight and of apparently the same constitution the same dose brings about no visible signs. The reason for this has been explained on the ground of individual susceptibility. Animal experimentation tends to show that the production of a marked degree of sensitization and the production of cutaneous manifestations are entirely separate phenomena. It is now well known[2] that complete anaphylactic shock (death) is more likely to follow reinjection after a small sensitizing injection of horse-serum, 0.1 to 0.00001, than after a large one, 10, 20 or 30 c.c. Such a comparatively small dose of horse-serum does not bring about an exanthem in man, but it does produce a specific change in the organism. Rosenau and Anderson believed this experience in animal experiments was due to an acquired immunity induced by the large amount of horse-serum injected. On the other hand, the somewhat more extended observations of Gay and Southard seem to show that the large initial dose, or the oft-repeated injections of moderate sized doses (2 to 5 c.c.), which in the aggregate total a large dose, give rise to a period of insusceptibility rather than to an immunity. For example, when they allowed a so-called incubation period of several weeks (thirty-eight to eighty-two days) to elapse, in guinea-pigs, after such initial doses, they found that instead of acting refractory they became characteristically sensitive, "the degree

2. Arthus 1903. Otto 1906. Rosenau and Anderson 1906.

of sensitivity varying directly with the time elapsed" since the primary injection.[3] A further observation bearing on this point is the suggestion of Hamburger and Moro that the precipitins bear a certain relation to the exanthem. They were unable to demonstrate precipitins in patients who had received only small doses of horse-serum, but demonstrated them with ease fourteen days after doses of from 10 to 20 c.c. We are able now, however, to show that while all patients do not exhibit signs of the disease up to the so-called threshold of cutaneous manifestation, their organism has undergone certain typical changes which can be demonstrated by biochemic reactions.

In 1903 Hamburger and Moro demonstrated precipitins for horse-serum in patients injected with large doses of horse-serum (Moser's scarlet fever serum), and the patients so injected showed a much more markedly positive reaction than those who had been injected with diphtheria antitoxin. The reason for this was that in the latter instance the amount of serum was small, while in the former a large amount, 10 to 20 c.c., of serum was used. They explain this phenomenon on the hypothesis that a larger amount of serum brings about a greater irritation of the cells, thus intensifying the reaction of the organism. Hamburger and Moro made the observation, referred to later, that the precipitins were demonstrable in the blood of injected children after the exanthem and not before, and propounded the much-quoted[4] theory, which they, however, abandoned in the same communication, namely, that the sudden appearance of antibodies and precipitins which enter the blood after a certain period of latency produce a binding of the precipitins to the biologically active groups of atoms of the free-coursing horse-serum. The precipitates thus formed produce through thrombosis of the capillaries circulatory disturbances which present themselves to the observer as exanthems. The researches of Rostoski, Michaelis and Openheimer, referred to by these writers, had definitely shown that

3. Besredka and Steinhardt applied the term anti-anaphylaxis to this phenomenon. Anderson and Rosenau in a later communication state that guinea-pigs sensitized with 0.01, 0.1, 1, and 8 c.c., respectively, showed no appreciable difference in the length of the incubation period. These animals were tested for oversensitiveness by intracerebral injection of horse serum (as first practiced by Besredka and Steinhardt). Gay and Southard in a paper published at the same time reaffirm their previous statement that the larger single dose or the oft-repeated dose of horse serum induces a longer incubation period.

4. Friedburger: Kritik der Theorien über die Anaphylaxie, Ztschr. f. Immunitätsf., 1909. ii, part 2, p. 212.

while such precipitation occurs in the test-tube when precipitable substance and precipitin are brought together, they do not so react within the living body. Hence, as Hamburger and Moro remark, this theory[5] had to be abandoned, a fact which many subsequent writers fail to recognize.

The idea that the precipitins entered the circulation suddenly after a certain period of latency, however, clung and was adhered to by Hamburger, von Pirquet and their coworkers for a long time. Much experimental work has centered around this point. Hamburger and Moro had determined the presence of precipitins for horse-serum in the blood of two children who had received 20 c.c. of Moser's scarlet-fever serum. In one, blood taken on the third day was negative, on the fourth day a general reaction occurred, exanthem and fever, two days later. Sixteen days after the injection the blood showed a strong reaction for precipitins. In another set of experiments three children were injected with 20, 10 and 20 c.c. horse serum, respectively. In the first precipitins appeared on the twenty-seventh day and continued until the thirty-first; in the second they appeared on the fifteenth day and continued until the twenty-ninth; and in the third they appeared on the thirteenth day and continued until the twenty-seventh.[6] In all cases the exanthem appeared in advance of the demonstration of precipitins (two to fifteen days). From such observations one could hardly fail to see an intimate connection between the phenomena which bring about exanthem and precipitin formation. It now remained to study more closely all these phenomena and perfect more accurate methods for determining the presence of these bodies in the blood-stream.

The following questions naturally arise: What happens to the horse-serum when it enters the body? Is it immediately split up or does it remain as such for a more or less definite time? Do precipitins and pre-

5. This theory calls to mind the work of Landois, who in 1875 demonstrated hemolysis of red blood corpuscles *in vitro* and *in vivo*, and who later showed that before the corpuscles are dissolved they are first agglutinated into clumps and thus may block large capillary areas (agglutination thrombi). After this, in the extraction of the hemoglobin by the hemolytic process, a further blocking of the capillaries is induced by the action of the hemoglobin on the leukocytes, setting the fibrin ferment free. Landois: Lehrb. d. Physiol. des Menschen, 1896; Die Transfusion des Blutes. Leipzig, 1875. Uhlenhuth: Ztschr. f. Hyg., 1897, xxvi. 384. Cited by Rosenau and Anderson.

6. These facts seem to have been overlooked by Rosenau and Anderson, hence some of their conclusions are incorrect.

cipitable substance exist side by side, and if so, for how long? Is it possible that the precipitins appear much earlier, before the exanthem?

The following observations may be cited in answer to the first question: Hamburger and Moro were acquainted with Ascoli's observation that injected egg albumin exists in the blood-stream for some time after injection, and Hamburger had demonstrated its presence four days after injection. With the same anti-horse-serum method Hamburger and Moro were able to demonstrate the presence of horse-serum in the blood-stream as late as thirty-one days after injection and to make the further observation that it (the precipitable substance) remains in most cases for only a short time after precipitins are found (in the first case four days, second five days, third two days). In animals injected with correspondingly large doses the precipitable substance was not demonstrated later than the sixth day and precipitins did not appear until the fifth to the eighth day.[7] They were not demonstrable after the tenth day. Hence in answer to our last question it will be seen that in both animals and children the precipitable substance and the precipitin exist side by side for a long time in the case of a child, for a very short period in the case of the rabbit.

Hamburger and von Pirquet (cited by von Pirquet and Schick, November, 1903) tested the serum of treated rabbits daily for precipitin formation. The precipitin never appeared earlier than the seventh day nor later than the tenth day after injection. They then waited for one or two months and repeated the injection. The new-formed precipitin now appeared earlier, between the fourth and fifth day. These findings von Pirquet and Schick attempt to explain in the following way: "The foreign serum does not act directly on the organism. The disease shows itself only when a change of the pathogenic substance has been effected, through the reaction product of the organism affected, and has reached a certain degree." They believe that the organism previously treated and injected a second time responds more quickly because the reaction products are still present in sufficient quantity (in which case we may assume an immediate reaction will take place) or the organism is able to produce reaction products more quickly than after a primary injection of serum. To this they apply the term "hastened reaction power."

7. Rosenau and Anderson failed to demonstrate precipitins in guinea-pigs after a single initial dose of horse serum because their animals had been treated thirty-five days previously; accordingly the precipitin stage had come and gone; and because the initial dose of serum was very small.

Von Pirquet and Schick saw an analogy between the cutaneous phenomena following reinjection of horse-serum and the tuberculin reaction. In addition to a so-called shortened incubation period there is produced an oversensitiveness. They state that this oversensitiveness "begins in the third week after the first injection, therefore, at about the time of the appearance of the precipitin." They tested patients injected with horse-serum very frequently from the day following injection until the symptoms disappeared, and their experience was the same as that of Hamburger and Moro; that is, the precipitins were never demonstrated before the exanthem, but always several days later, and in some instances continued into the ninth week. The earliest positive precipitin reactions in eight cases examined were obtained during the third week (three cases, Nos. 2, 5, 6). These observations threw no new light on the question of the relationship of precipitin formation to exanthems. Von Pirquet and Schick, while unable to detect any direct relationship between precipitins and exanthems, nevertheless admit a possible connection between the two.

Dehne and Hamburger, from a series of precipitin experiments, came to the conclusion (1907) that the symptoms of serum sickness are accompanied by a temporary diminution of the precipitable substance. The precipitins which have been formed (first formed) are immediately bound to the precipitable substance. From this work Hamburger and Pollak draw the conclusion that the diminution of the precipitable substance is only the consequence of the precipitin formation which has taken place, that is, the precipitins which are formed are immediately bound by the precipitable substance, and for this reason it is impossible to demonstrate their presence directly until they have been formed in abundance. They therefore argue that because they were unable to detect precipitins until several days had elapsed, it does not prove that they are not there and that they have no causal relation to serum sickness as has been assumed by von Pirquet and Schick. On the contrary, they remark "the very coincidence in time of the demonstration of the precipitable substance and the occurrence of serum sickness symptoms speaks for a causal rôle for the precipitins, or the antibodies formed simultaneously with them." On this reasoning Hamburger and Pollak assumed that in all probability, if precipitin formation could be demonstrated as early as the fourth or fifth day (Dehne and Hamburger),

and if together with this there was a diminution of the precipitable substance, the specific sensitiveness to horse-serum should become demonstrable much earlier than the appearance of the symptoms of serum sickness proper. They introduced the intracutaneous test to determine if this was so. It will be recalled that von Pirquet and Schick drew attention to the time relationship of the appearance of precipitins and the symptoms of oversensitiveness. Thus far evidence tends to show, in answer to our last question, that the precipitins appear in advance of the exanthem.

By use of intradermal injections Hamburger and Pollak were able to demonstrate that specific oversensitiveness is present as a rule on the fifth or sixth day after a primary injection of horse-serum, and that it increases in intensity up to the fourteenth day, when the highest degree of reaction is attained—*specific edema.* Arthus had previously made parallel observations on rabbits. These were apparently unknown to Hamburger and Pollak. To this highest degree of reaction von Pirquet and Schick gave the term specific edema. In work of this character the importance of ruling out coreactions, for example, those which occur after a second dose of tuberculin, must be borne in mind.

Not all children who are treated with horse-serum react to the intradermal test. Out of fifty children treated by Hamburger and Pollak, one was found to be refractory. Even after repeated injections of horse-serum over a period of twelve days, no reaction was obtained. These observations seem to show quite conclusively that the oversensitiveness increases gradually. In some cases they were able to obtain a slight reaction on the second day, and successive reactions increasing in intensity until the sixth day. Hamburger and Pollak concluded from these experiments that the degree of specific serum oversensitiveness increases relatively, and that during this time clinical signs may or may not be present. They suggest that the increase of oversensitiveness probably depends on the increase in antibodies (precipitins). In some cases the oversensitiveness was so marked that serum diluted 1 to 1,000 gave a reaction. They assume that during the clinical incubation period antibodies have been present in the blood for a long time, but their number has not been sufficient to produce clinical symptoms, and that the antibodies increase in geometrical rather than in arithmetical progression.

AUTHOR'S EXPERIMENTS

Series I.

Successive Intradermal Injections following Prophylactic Injections of Diphtheria Antitoxin.

The object of these experiments was to determine in as many cases as possible the time at which specific oversensitiveness to horse-serum could first be demonstrated; in other words, the time that elapses from the first injection of horse-serum until antibodies are demonstrable by the intracutaneous test.

Method.—Small intradermal injections of 0.5 c.mm. (½cm.³) diphtheria antitoxin or normal horse serum were made at frequent intervals following the primary injection of antitoxin. A fine sharp polished hypodermic needle attached to a 1 c.c. glass syringe graduated in hundredths was used for the injections. The bulk of fluid injected was, within narrow limits, always the same. The serum was not diluted. This assured a response if oversensitiveness had been reached to the point of showing a visible change in the skin. Control tests with sterile water, salt solution, and dry sterile needle done many times, enabled me to determine quite closely the difference between a traumatic and a specific reaction. The injections, as the term denotes, were made into and not beneath the skin; as close to the surface as possible. A proper injection shows a whitish circular elevation from 5 to 7 mm. in diameter by 1 mm. in height with a miliary dimpled top showing that the subepidermoidal tissue is infiltrated with the serum.

The point of inoculation in the interscapular space (back), together with the sites of intradermal injection, was observed day by day. It gave knowledge as to whether oversensitiveness showed itself during the first twenty-four hours after injection as well as knowledge of a peculiarity not present in all cases — that of a marked cutaneous reaction in its vicinity which occurs after oversensitiveness is reached.

The intradermal method is more reliable for this work than the scratch, or the boring method of v. Pirquet. We are always assured that a definite amount is given to and retained by the skin. (A word of caution: this method must not be employed in making the cutaneous tuberculin test. The absorption is too great and the dilutions usually made carry large doses of tuberculin. Even the normal body may react with marked and painful symptoms.)

Intradermal injections of horse serum made for the first time bring about no visible reaction in the skin until the "clinical incubation period" is passed.

EXPERIMENTS

CASE 1.—Dean S., aged 6 months. May 23, 1912, received 1,000 units diphtheria antitoxin in interscapular space.

Day 1—May 24. First intradermal in left arm 0.5 cm.³
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back neg. Second intradermal in left arm 0.5 cm.³
Day 4—May 27. Arm and back neg. Third intradermal in left arm 0.5 cm.³
Day 5—May 28. Arm and back negative.
Day 6—May 29. Arm and back neg. Fourth intradermal in left arm 0.5 cm.³

Day 7—May 30. 1, 2, 3 and back negative; 4, red area 5 cm. in diameter.
Day 8—May 31. 1, 2, 3 and back negative; 4 fading.
Day 9—June 1. All negative. Fifth intradermal in right arm.
Day 10—June 2. 1, 2, 3 and 4 negative; 5 red area 6 by 4 cm.
Day 11—June 3. Fifth, fading.

CASE 2.—John C., aged 6 months. Congenital lues. May 23 was given 100 units diphtheria antitoxin for the first time in the interscapular space.

Day 1—May 24. First intradermal in arm 0.5 cm.^{3}
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative. Second intradermal 0.5 cm.^{3}
Day 4—May 27. Arm and back negative. Third intradermal 0.5 cm.^{3}
Day 5—May 28. 1, 2 and back negative; 3 hyperemic 5 mm. diam., trauma.
Day 6—May 29. 1, 2 3 and back negative; 4 intradermal 0.5 cm.^{3}
Day 7—May 30. Arm and back negative.
Day 8—May 31. Arm and back negative.
Day 9—June 1. Arm and back negative; 5 intradermal 0.5 cm.^{3}
Day 10—June 2. Arm and back negative.
Day 11—June 3. Arm and back negative.
Day 40—July 13. Sixth intradermal.
Day 41—July 14. Distinct characteristic pink reaction 7 mm. in diameter.
Day 42—July 15. Negative.

CASE 3.—Zena B., aged 8 months. Orthopedic case. May 23 received 100 units diphtheria antitoxin in interscapular space for the first time.

Day 1—May 24. First intradermal 0.5 cm.^{3} in arm.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative. Second intradermal 0.5 cm.^{3} in arm.
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.^{3} in arm.
Day 5—May 28. 1, 2 and back negative; 3 faint hyperemia.
Day 6—May 29. 1, 2 and back negative; 3 faint as before; 4 intradermal 0.5 cm.^{3} in thigh.
Day 7—May 30. 1, 2, 3 and back negative; 4 red area on thigh 1 cm. in diam.
Day 8 May 31. 1, 2, 3 and back negative; 4 erythema 1.5 cm. in diameter.
Day 9—June 1. All negative; 5 intradermal 0.5 cm.^{3} serum in thigh.
Day 10—June 2. 1, 2, 3, 4 and back negative; 5 on thigh very red area 1 cm. in diameter.
Day 11—June 3. All negative.

CASE 4.—Katherine J., aged 9½ months. May 23 was given 1,000 units of diphtheria antitoxin in the interscapular space for the first time.

Day 1—May 24. First intradermal injection 0.5 cm.^{3} serum, left arm.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.^{3}, left arm.
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.^{3}, left arm.
Day 5—May 28. 1, 2 and back negative; 3 shows characteristic hyperemia 1 cm. in diameter.
Day 6—May 29. 1, 2 and back negative; 3 fading; 4 intradermal given, 0.5 cm.^{3} right arm.
Day 7—May 30. 1, 2, 3 and back negative; 4 shows a red area 1 cm. in diam.
Day 8—May 31. 1, 2, 3 negative; 4 fading.
Day 9—June 1. Fifth intradermal 0.5 cm.^{3}, right thigh. All negative.
Day 10—June 2. 1, 2, 3, 4 neg.; 5, 2 by 1 cm. hyperemia.
Day 11—June 3. All negative.

CASE 5.—Melville W., aged 1½ years. May 23 was given 1,000 units of diphtheria antitoxin in the interscapular space.

Day 1—May 24. First intradermal on arm 0.5 cm.³
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal in arm 0.5 cm.³
Day 4—May 27. Arm and back negative; 3 intradermal in arm 0.5 cm.³
Day 5—May 28. 1, 2, arm and back negative; 3 red indurated area 0.5 cm. in diam.; looks like trauma.
Day 6—May 29. 1, 2, 3 and back negative, 4 intradermal in arm 0.5 cm.³
Day 7—May 30. 1, 2, 3, 4 and back negative.
Day 8—May 31. 1, 2, 3, 4 and back negative.
Day 9—June 1. 1, 2, 3, 4 and back neg.; 5 intradermal in thigh 0.5 cm.³
Day 10—June 2. 1, 2, 3, 4 and back negative; 5 on thigh faintly positive. June 3, all negative.

CASE 6.—Noel B., aged 3½ years. Chronic meningitis. May 23, 1912, was given 1,000 units of diphtheria antitoxin in the interscapular space. May 24 intradermal injection of 0.5 cm.³ serum was given in arm.

Day 1—May 25. No reaction in arm or back.
Day 2—May 26. A second intradermal injection of 0.5 cm.³ below the first.
Day 3—May 27. No reaction occurred. A third intradermal 0.5 cm.³ given.
Day 4—May 28. No reaction at site of first intradermal or back. Questionable reaction at site of second intradermal. Area 1 cm. in diameter; hyperemia at site of third intradermal.
Day 5—May 29. Back negative. Fourth intradermal given. Site of first intradermal negative. Site of second intradermal a pink area of hyperemia 2.5 cm. in diameter with a yellowish center. No induration. Site of third intradermal deeper red hyperemia 2.5 cm. in diam.
Day 6—May 30. First intradermal and back negative. Second intradermal bright red hyperemia 2.5 by 5 cm. in diam. Third intradermal negative. Fourth intradermal deep red area 0.5 cm. in diam.
Day 7—May 31. Back negative. First intradermal negative. Second intradermal red area 4 by 3.5 cm. in diam. Third and fourth fused, forming a red indurated area 6 by 7.5 cm.
Day 8—June 1. Back negative; 1 and 2 negative; 3 and 4 same size as yesterday, but fading. A fifth intradermal of 0.5 cm.³ given in thigh.
Day 9—June 2. 1, 2, 3 and 4 all faint, probably from fusing of 3 and 4 (all in arm); 5 on thigh 3.5 by 3.5 cm. area of bright red.
Day 10—June 3. All negative.

CASE 7.—Earl S., aged 4 years. Orthopedic. May 22, 1912, was given 1,000 units of diphtheria antitoxin in the interscapular space for the first time.

Day 3—May 25. First intradermal 0.5 cm.³ serum in arm.
Day 4—May 26. Arm and back negative; 2 intradermal 0.5 cm.³ in arm.
Day 5—May 27. All negative.
Day 6—May 28. 1, 2 and back negative. Third intradermal 0.5 cm.³ in arm.
Day 7—May 29. 1, 2, 3 and back negative; 4 intradermal 0.5 cm.³ in arm.
Day 8—May 30. 1, 2, 3 and back negative; 4 questionable area 5 cm. in diam.
Day 9—May 31. All negative.
Day 10—June 1. All negative. Fifth intradermal.

Day 11—June 2. 1 and back negative; 2, 3 and 4 show characteristic red areas; 5 shows a red slightly indurated area on the thigh 2 by 3 cm.

Day 12—June 3. All very positive with slight itching; no induration; 5, 4 by 4 cm.

Day 13—June 4. All on arm very marked. Urticaria on right leg and left face. Fifth on thigh fading.

CASE 8.—Clifford H., aged 4 years. Tuberculous knee. Had 1,000 units antitoxin ten weeks ago. May 23, 1912, given a second dose of 1,000 units in interscapular space.

Day 1—May 24. First intradermal in left arm 0.5 cm.^{3}

Day 2—May 25. Arm shows beginning diffuse redness 1 cm. in diameter. Back shows a similar area around point of injection.

Day 3—May 26. Redness on arm and back fading; 2 intradermal in arm 0.5 cm.^{3}

Day 4—May 27. 1 and back negative; 2 positive red area, not measured; 3 intradermal in arm 0.5 cm.^{3}

Day 5—May 28. 1 and back negative; 2 very red area 5.5 cm. in diameter with yellowish center 1 cm. in diameter, but irregular. Area about 4 cm. in diameter, irregular central portion, yellowish wheal, periphery bright red hyperemia with irregular border.

Day 6—May 29. Back negative; 1, 3.5 cm. in diameter, mottled rose red area; 2, 4 cm. in diameter, fairly uniform redness, with yellow center about 0.5 cm.; 3, 4 cm. in diameter, pale center about 5 cm. in diameter, with a rich bright rose periphery; 4, intradermal in arm 0.5 cm.^{3}

Day 7—May 30. Back negative; 1, 4 by 5 cm. in diameter; mottled; 2, 5 by 5 cm. in diameter, fine pink mottling; 3, 5 by 4.5 cm., fine pink mottling; 4, 5.5 by 4.5 cm. in diameter, deeper red, particularly around the periphery, with slight induration.

Day 8—May 31. Back negative; 1, 5.5 by 5 cm., fading, but markedly mottled; 2, 5.0 by 4.5 cm., marked redness; 3, 5.5 by 5 cm., very marked red mottling; 4, 4.0 by 6 cm., uniform redness, no induration.

Day 9—June 1. All about the same size, but all are fading; 5 intradermal 0.5 cm.^{3} in thigh and other arm.

Day 10—June 2. All positive, brighter than yesterday; 4 and 5 fused, forming a red area 6 by 9 cm., with urticaria lesions above; 5 on right arm positive.

Day 11—June 3. All on left arm negative; right arm erythema 6 by 6 cm. See Fig. 1.

Day 40—July 13. 6 intradermal at two points, about 1.5 cm. apart.

Day 41—July 14. Both show an inner area 7 by 12 mm., irregular red and an outside diffuse fusing area 50 by 65 mm.

Day 42—July 15. All negative.

Day 146—Nov. 27. Intradermal 0.5 cm.^{3} in right arm.

Day 147—Nov. 28. Mottled area 9 by 5 mm., faint pink becoming marked rose red on gentle rubbing. There are a few elevated points, but no distinct urticaria; induration. Back negative.

Day 148—Nov. 29. Area 10 by 3 mm., distinctly mottled rose red.
Day 149—Nov. 30. Area fading, almost invisible.
Day 151—Dec. 2. There is an erythematous mottling 10 by 5 mm., and marked itching this morning. There is one marked wheal but no general induration of the area.
Day 152—Dec. 3. The arm is entirely negative. Redness not excited by gentle rubbing.

Fig. 1.—Clifford H. Case 8. Showing the reappearance of a reaction at the site of the first intradermal injection (1). On the previous day this area was entirely negative, while two and three were positive; three had been made twenty-four hours previously, but had induced no reaction at one until after forty-eight hours, at which time the picture was taken. See text page 264.

Day 153—Dec. 4. Negative.
Day 156—Dec. 7. Arm negative; 8 intradermal, 0.5 cm.^{3} in left arm.
Day 158—Dec. 9. There is a fading area 4 mm. in diameter.
Day 159—Dec. 10. Greenish discoloration 4 cm. in diameter.

Day 285—Apr. 15. 9 intradermal.
Day 286—Apr. 16. Very marked reaction, swelling and erythema over entire flexor surface of forearm.
Day 287—Apr. 17. Erythema continues with several large urticarial wheals.

CASE 9.—Harold S., aged 5 years. Was given 1,000 units diphtheria antitoxin May 23 in the interscapular space. First antitoxin.

Day 1—May 24. First intradermal in arm 0.5 cm.^{3}
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative. Second intradermal in arm 0.5 cm.^{3}
Day 4—May 27. 1 and 2 show distinct redness. Back negative. Third intradermal 0.5 cm.^{3}
Day 5—May 28. 1 negative; 2 very red hyperemic area. 7 mm. in diameter, yellow center; 3 similar area 5 cm. in diam.; wheal-like center.
Day 6—May 29. Back negative; 4 intradermal left thigh 0.5 cm.^{3}; 1 negative; 2 almost invisible area 2.5 cm. in diameter; 3 almost invisible area 1.25 cm. in diameter.
Day 7—May 30. 1, 2, 3 and back negative; 4, slightly indurated red area on left thigh 1 cm. in diameter.
Day 8—May 31. 1, 2, 3 and back negative; 4, 2 cm. in diameter, uniform red.
Day 9—June 1. 1, 2, 3 and 4 negative; 5 intradermal 0.5 cm.^{3}
Day 10—June 2. 1, 2, 3, 4 and back negative; 5 shows hyperemic area 6 by 5 cm.; no induration.
Day 11—June 3. 1, 2, 3, 4 and 5 negative.

CASE 10.—Joe K., aged 5 years. May 23 was given 1,000 units of diphtheria antitoxin in the interscapular space. First antitoxin.

Day 1—May 24. First intradermal in left arm 0.5 cm.^{3} serum.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.^{3}
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.^{3}
Day 5—May 28. 1, 2, 3 and back negative.
Day 6—May 29. 1, 2, 3 and back negative; 4 intradermal 0.5 cm.^{3}
Day 7—May 30. Back negative; 1 faint reaction, 1 cm. in diameter; 2 bright red area, 2.5 by 3.5 cm.; 3 bright red area, 2.5 by 2.5 cm.; 4 indurated, itching red area 2 by 4.5 cm.
Day 8—May 31. Back negative; 1, 2.5 by 3 cm., fading red area, yellow center; 2 area fading, 3 by 3 cm.; 3 almost entirely faded; 4 red, slightly indurated area, 5 by 4 cm.
Day 9—June 1. Back negative; 1, 2, 3 and 4 negative; 5 intradermal 0.5 cm.^{3} in thigh.
Day 10—June 2. Back negative; 1, 2, 3 and 4 negative; 5 faint red area, 3 by 4 cm. in diameter, on thigh.
Day 11—June 3. 1, 2, 3, 4, 5 and back negative.

CASE 11.—Ruth F., aged 5 years. May 23 was given 1,000 units of diphtheria antitoxin for the first time in the interscapular space.

Day 1—May 24. First intradermal injection 0.5 cm.^{3} serum.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.^{3}
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.^{3}

Day 5—May 28. 1, 2 and back negative; 3 shows characteristic hyperemia 0.5 cm. in diameter.
Day 6—May 29. 1 and back negative; 4 intradermal 0.5 cm.^{3}; 2 fusing with 3; 3 shows hyperemia 1 cm. in diameter.
Day 7—May 30. 1, 2, 3 and back negative; 4 red area 1.5 cm. in diameter.
Day 8—May 31. 1, 2, 3 and back negative; 4 still very positive, 2.5 cm. in diameter, but fading. Patient left hospital.

CASE 12.—Lulu Q., aged 6 years. Diphtheria. May 23 was given 1,000 units of diphtheria antitoxin for the first time.

Day 1—May 24. First intradermal injection 0.5 c.c. in arm.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.^{3}
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.^{3}
Day 5—May 28. Arm and back negative.
Day 6—May 29. Arm and back negative; 4 intradermal 0.5 cm.^{3}
Day 7—May 30. 1, 2 and back negative; 3 shows a pink mottled area 2.5 cm. in diameter; 4 similar pink area fusing with 3 began to appear last evening; 3 did not get red until this morning.
Day 8—May 31. 1, 2, 3, 4 and back negative.
Day 9—June 1. 1, 2, 3, 4 and back negative; 5 intradermal injection, 0.5 cm.^{3}
Day 10—June 2. All negative.
Day 11—June 3. All negative.

CASE 13.—Louise O., aged 6 years. Fracture case. May 23 was given 1,000 units of diphtheria antitoxin for the first time.

Day 1—May 24. First intradermal 0.5 cm.^{3} in arm.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal in arm. 0.5 cm.^{3}
Day 4—May 27. 1, 2 and back negative; 3 intradermal in arm.
Day 5—May 28. 1, 2 and back negative; 3 hyperemia 0.5 cm. in diameter (traumatism); 4 intradermal in arm; 0.5 c.c.
Day 6—May 29. 1, 2, 3 and 4 negative.
Day 7—May 30. 1, 2, 3 and 4 negative. Back shows an area 2.5 cm. in diameter at site of injection. Erythema over both knees. (Serum sickness.)
Day 8—May 31. 1, 2, 3, 4 and back negative.
Day 9—June 1. One and back negative; 2, 3 and 4 positive; 5 intradermal.
Day 10—June 2. All negative.
Day 11—June 3. All negative.
Day 12—July 13. Sixth intradermal.
Day 13—July 14. Negative.
Day 14—July 15. Negative.
Day 149—Nov. 27. Sixth intradermal 2 cm^3 diphtheria antitoxin.
Day 150—Nov. 28. There is a mottled area 10 by 5 mm. made up of red blotches. There are no elevated spots. The red area is increased in intensity by gently rubbing.
Day 151—Nov. 29. The point of injection is negative. Not excited by rubbing.
Day 152—Nov. 30. The point of injection is negative. Not excited by rubbing.
Day 154—Dec. 2. The point of injection is negative. Not excited by rubbing.
Day 155—Dec. 3. The point of injection is negative. Not excited by rubbing.

CASE 14.—James H., aged 7 years. May 23 was given 1,000 units diphtheria antitoxin in the interscapular space. First antitoxin.

Day 1—May 24. First intradermal in arm 0.5 cm.³
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.³ serum.
Day 4—May 27. 1, 2 and back negative; 3 intradermal 0.5 cm.³
Day 5—May 28. 1, 2, 3 and back negative.
Day 6—May 29. 1, 2, 3 and back negative; 4 intradermal 0.5 cm.³
Day 7—May 30. 1, faint mottling around point of injection, back negative; 2, 3 negative; 4 pink, slightly indurated area 2.5 cm. in diameter.
Day 8—May 31. 1, 2 and back negative; 3 fading, almost invisible; 4 area 3 by 4 cm., fading.
Day 9—June 1. 1, 2, 3 and back negative; 4 fading; 5 intradermal 0.5 cm.³ in thigh.
Day 10—June 2. 1, 2, 3, 4 and back negative; 5, 2.5 cm. in diameter, red hyperemic area.
Day 11—June 3. All negative.

CASE 15.—Agnes B., aged 9 years. May 23 received 1,000 units of diphtheria antitoxin for the first time.

Day 1—May 24. First intradermal injection 0.5 cm.³ serum.
Day 2—May 25. Arm and back negative.
Day 3—May 26. Arm and back negative; 2 intradermal, 0.5 cm.³
Day 4—May 27. Arm and back negative; 3 intradermal, 0.5 cm.³
Day 5—May 28. 1, 2, 3 and back negative; 4 intradermal, 0.5 cm.³
Day 6—May 29. Back shows a slightly elevated and indurated area over site of injection 5 by 2 cm. in diameter, one or two wheals; 1 negative; 2 shows a red mottling 1.5 cm. in diameter; 3 similar mottling, 2 cm. in diameter; 4 faint pink area 2 by 2.5 cm.
Day 7—May 30. Back negative; 1, 2 and 3 fused, 10.5 by 4 cm.; 4 shows an area of urticaria 4 cm. in diameter.
Day 8—May 31. Back negative; 1, 2 and 3 fused as above, but not so red; 4 shows redder area this morning 5 by 4 cm.
Day 9—June 1. Back negative; 1, 2 and 3 fading; 4 on thigh shows an area of redness 10.5 by 5 cm.; fifth intradermal injection, 0.5 cm.³, given one hour ago, shows a hyperemic area 2.5 cm. in diameter.
Day 10—June 2. 1, 2, 3, 4 negative; 5 faint area 4 by 2.5 cm.; back negative.
Day 11—June 3. 1, 2, 3, 4 and back negative; 5 shows a faint area of erythema 10 cm. in diameter.
Day 12—June 4. Slight erythema over knees. (Operated yesterday p. m.)

CASE 16.—Crystal B., aged 11 years. May 23 was given 1,000 units diphtheria toxin for the first time.

Day 1—May 24. First intradermal 0.5 cm.³ serum.
Day 2—May 25. Arm and back negative.
Day 3.—May 26. Arm and back negative; 2 intradermal 0.5 cm.³
Day 4—May 27. Arm and back negative; 3 intradermal 0.5 cm.³
Day 5—May 28. 1 and back negative; 2 bright red irregular mottled area 1 cm. in diameter; 3 marked pink mottled area with uniform pink center and small macular spots around, hyperemic 1.5 cm. in diameter.

Day 6—May 29. Back negative; 1 mottled area 1.5 cm. in diameter, pink; 2 deep hyperemic pink area with light center 2 cm. in diameter; 3 deep pink hyperemic area with pale center 4 by 3 cm. in diameter; 4 intradermal 0.5 cm.³

Day 7—May 30. Back negative; 1 mottled red area 2 cm. in diameter; 2 uniform red area, 2 cm. in diameter; 3 uniform red area 3 by 4 cm.; 4 on thigh deep red slightly indurated area 3 cm. in diameter; marked itching in the arm.

Day 8—May 31. Back negative; 1 fading; 2 fading; 3 fading; all still red and mottled; 4 red area 4 by 3 cm.

Day 9—June 1. 1, 2, 3 same as yesterday; back negative; 4 same as yesterday; 5 intradermal 0.5 cm.³ serum. An hour later a red area 4 by 2.5 cm.

Day 10—June 2. 1, 2, 3 and back negative; 4 area 3 cm. in diameter, fading; 5 bright red area 6 cm. in diameter, no induration.

Day 11—June 3. 1, 2 and 3 have brightened up a distinct faint red and macular; 4 red area 4 by 4 cm. in diameter; 5 bright red hyperemia 7.5 by 5 cm.

Day 12—June 4. Erythema continues on both arms. (Operated in surgical clinic yesterday.)

CASE 17.—Adrian W., aged 13 years. May 22, 1912, was given 1,000 units of diphtheria antitoxin in the interscapular space.

Day 3—May 25. First intradermal 0.5 cm.³ serum.

Day 4—May 26. Arm and back negative; 2 intradermal 0.5 cm.³ serum.

Day 5—May 27. Arm and back negative.

Day 6—May 28. Back negative; 1 shows faint pink area 2.5 cm. in diameter with yellow center; 3 intradermal 0.5 cm.³ serum; 2 shows an area 2.5 cm. in diameter, bright pink, macular.

Day 7—May 29. 1 and back negative; 2 fading; 3 same size, red and indurated; 4 intradermal injection in thigh, 0.5 cm.³

Day 8—May 30. 1 and back negative; 2 mottled and fading; 3, 3 by 2.5 cm., pink; 4, 4.5 by 3 cm., red induration; 3 and 4 itching, 3 began to itch several hours before 4. Slight itching at puncture wound in back.

Day 9—May 31. 1, 2 and back negative; 3 fading; 4 uniform pink area, slightly indurated, 5 by 6.5 cm.

Day 10—June 1. All negative. Fifth intradermal 0.5 cm.³ in thigh.

Day 11—June 2. 1, 2, 3, 4 and back negative; 5 shows a faint pink area 2.5 cm. in diameter.

Day 12—June 3. All negative.

CASE 18.—Miss O., aged 21 years. May 23, 1912, was given 2,000 units of diphtheria antitoxin in the interscapular space for the first time.

Day 2—May 25. First intradermal in arm 0.5 cm.³ serum.

Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.³ in arm.

Day 4—May 27. Arm and back negative.

Day 5—May 28. Back negative; 1 shows an irregular blotchy marked redness without induration 3 by 2.5 cm.; 2 same; 3 intradermal 0.5 cm.³ serum in arm.

Day 6—May 29. Back negative; 1 shows uniform redness 3 cm. in diameter; 2 similar redness 5.5 cm. in diameter; 3 similar redness 5 by 4 cm. in diameter. fusing with 2.

Day 7—May 30. 1, 2, 3 positive; back negative; slight signs serum sickness.
Day 8—May 31. 1, 2, 3 fading; back negative.
Day 9—June 1. 1, 2, 3 fading, back negative; 4 intradermal 0.5 c.c. serum.
Day 10—June 2. 1, 2, 3 positive; 4, 7.5 cm. in diameter, all bright red; back negative.

CASE 19.—Miss C., aged 21 years. May 23 was given 2,000 units of diphtheria antitoxin for the first time in the interscapular space.

Day 2—May 25. First intradermal 0.5 cm.^{3} serum in arm.
Day 3—May 26. Arm and back negative; 2 intradermal 0.5 cm.^{3} in arm.
Day 4—May 27. 1, 2 and back negative.
Day 5—May 28. 1 faint pink area 2.5 cm. in diameter; 2 uniform red area 2.5 cm. in diameter. Back shows an irregular blotchy redness around site of injection 2.5 cm. in diameter; 3 intradermal 0.5 c.c. serum.
Day 6—May 29. Back negative; 1 faint diffuse redness; 2 red area 4 cm. in diameter; 3 reported as very large last night. This morning shows a red indurated area 2 cm. in diameter; 4 intradermal 0.5 c.c. in arm.
Day 7—May 30. 1 and back negative: 2 area 4.5 by 4.5 cm.; 3 area 6 by 4 cm.; 4 area 5 by 5 fusing with 3, marked induration. Patient says that just as one spot begins to disappear it starts to itch. Second itching to-day; first has stopped.
Day 8—May 31. 1, 2 and back negative: 3 and 4 fading.

CASE 20.—Mrs. R., April 23, 1912, was given 1,000 units diphtheria antitoxin in the interscapular space for the first time.

Day 7—April 30. 9:30 a. m., 15 minims serum was given intradermally in the left arm. There is a reddened itching area 12 by 12 inches over back of right shoulder in region of original inoculation: 7 p. m., 6 by 4 inches in diameter over the arm; very marked redness and infiltration, which is sharply defined, with whitish center, itching.
Day 8—May 1. 8:30 a. m., reddened area over whole upper arm; infiltration more marked; itching; 4:30 p. m., no change in appearance, but the arm is more tender.

CASE 21.—Mrs. P. April 23, 1912, 1,000 units of diphtheria antitoxin given in the interscapular space for the first time.

Day 7—April 30. 9:30 a. m., 15 minims of serum intradermally in the left upper arm; 7:00 p. m., slight reddening and infiltration about area of injection.
Day 8—May 1. 8:30 a. m., reaction is more marked, redder; more infiltration, itching at point of injection and under arm. 11:00 a. m., redness increasing, rubbing over the area of injection in the back produces redness. Rubbing on the opposite side produces no redness. 4:30 p. m., the area on arm has become tender, itches and shows a secondary areola.

CASE 22.—Mrs. M. April 23, 1912, was given 1,000 units of diphtheria antitoxin in the interscapular space for the first time.

Day 7—April 30. 9:30 a. m., 8 minims of serum given intradermally in left arm. Noon, urticarial eruption about site of original injection in the back, with itching. 7:00 p. m., slight urticarial area above point of injection on arm.

Day 8—May 1. 8:30 a. m., reaction more marked, redder, very little infiltration. 11:00 a. m., 4 cm. in diameter on arm. Infiltration and hyperemia more marked, tenderness, no itching. No urticaria on back, but a diffuse redness 10 by 5 cm. 4:30 p. m., no change.

Day 9—May 2. Patient complained of itching over the back and chest during the night.

CASE 23.—Mrs. B. April 23, 1912, 1,000 units of diphtheria antitoxin in interscapular space for the first time.

Day 7—April 30. 9:30 a. m., 8 minims of serum intradermally left upper arm. 7:00 p. m., there is an area of urticaria 6 by 6 inches the site of original injection; also an area of reddening and marked infiltration 4 by 3 inches on left upper arm.

Day 8—May 1. 8:30 a. m., the reaction on the back has decreased. The area on the arm has increased, but the infiltration is less marked. 4:30 p. m., still less infiltration. The area over the arm is blotchy red in character and itching. Patient discharged before another observation could be made.

CASE 24.—Mrs. P. A. April 23, 1912, 1,000 units diphtheria antitoxin in the interscapular space for the first time.

Day 7—April 30. 9:30 a. m., 15 minims of serum in left arm intradermally; 7:00 p. m., negative.

Day 8—May 1. 8:30 a. m., diffuse red area with infiltration, itching and tenderness 5 by 8 cm. over arm; 4:30 p. m., no change; 2 more diffuse redness. Line of infiltration less defined. 3, reaction more marked, more diffuse. No note on back.

CASE 25.—Mrs. Pal. April 23, 1912, 1,000 units diphtheria antitoxin for the first time in the interscapular space.

Day 7—April 30. 9:30 a. m., 15 minims of serum intradermally in left arm. 7:00 p. m., there is a swollen faint red infiltrated area 10 by 5 cm. over arm.

Day 8—May 1. 8:30 a. m., reaction same as last night. Redness produced on slight rubbing. Slight flush about original injection in back. 4:30 p. m., infiltration marked. Tender but no larger.

Day 9—May 2. Reaction less noticeable. Some itching.

Day 10—May 3. Reaction has disappeared.

CASE 26.—Mrs. T. April 23, 1912, 1,000 units diphtheria antitoxin for the first time in back.

Day 7—April 30. 9:30 a. m., 8 minims of serum in left upper arm intradermally. 7:00 p. m., slight tenderness about point of injection on arm; no other reaction.

Day 8—May 1. 8:00 a. m., no change. 11:00 a. m., there is a raised infiltrated area on the arm 4 by 4 cm.; on the back there is diffused urticarial eruption. 4:30 p. m., same as last note.

Day 9—May 3. Reaction has disappeared.

CASE 27.—Mrs. H. April 23, 1912, 1,000 units of diphtheria antitoxin in left flank for the first time.

Day 7—April 30. 9:30 a. m., 8 minims of serum intradermally in left upper arm. 7:00 p. m., there is an area of infiltration and itching 5 by 3 cm. about the point of injection on arm. There is also a red rash about the original point of injection in left flank.

Day 8—May 1. 8:30 a. m., area on arm redder, more infiltrated 7.5 by 5 cm.; flank remains same.

Day 9—May 2. The area on the arm is more diffuse at 11 a. m., 6 by 10 cm., and redder.

Day 10—May 3. Area on arm still more diffuse. No note on flank.

CASE 28.—Mrs. W. April 23, 1,000 units of diphtheria antitoxin in back for first time.

Day 9—May 2. 7:00 p. m., 10 minims intradermally in upper right arm.

Day 10—May 3. 9:00 a. m., there is an area of slight swelling on the arm 5 by 8 cm., with very little redness. 3:30 p. m., the reaction is more marked, more diffuse; very little infiltration and redder. No note on back.

CASE 29.—Mrs. H. A. April 23, 1,000 units of diphtheria antitoxin in back for first time.

Day 5—April 28. 8:00 p. m., there is an area on the right shoulder 8 by 8 cm., just above point of injection of antitoxin. Slightly swollen, red and itching. (Nurse's note.)

Day 6—April 29. Area on right shoulder still red but swollen. (Nurse's note.)

Day 9—May 2. 7 minims of serum, intradermally in left upper arm.

Day 10—May 3. 9:00 a. m., there is an area of marked redness and infiltration 5 by 8 cm., over point of injection on arm.

Day 11—May 4. 3:30 p. m., no change. No note about back.

CASE 30.—Miss W., May 1, 1912, 1,000 units of diphtheria antitoxin in back for the first time, 4:30 p. m.

Day 3—May 4. 9 a. m., 8 minims of serum intradermally in left arm; 7 p. m., no reaction. Patient discharged; no further observations could be made.

Note.—I am indebted to my staff assistant, Mr. Paul Schule, for observations on the adult cases, most of which I confirmed.

ANALYSIS OF OBSERVATIONS; SERIES I

Thirty individuals whose ages varied from 6 months to middle adult life were sensitized to horse-serum by means of prophylactic injections of diphtheria antitoxin. Of these, seventeen were children and thirteen adults. Ninety-four per cent. of these cases reacted to the cutaneous test. One of the children (No. 2) was found to be refractory; that is, after repeated intradermal injections sensitization could not be demonstrated up to the tenth day of the experimental period. However, specific oversensitiveness was demonstrated in this case on the forty-

first day. One adult (30) did not remain long enough for specific sensitiveness to occur and accordingly cannot be counted in the total. One hundred per cent. of the adults responded to the test; 94 per cent. of the children. (See later notes on these cases.)

Time of Reaction.—Of the nineteen cases which were closely observed specific oversensitiveness was first demonstrable on the

Second day in	1 case*
Fourth day in	1 case
Fifth day in	7 cases
Sixth day in	1 case
Seventh day in	5 cases
Ninth day in	1 case
Tenth day in	2 cases
No reaction in	1 case
Total	19 cases

* No. 8 reinjection case.

Duration of Reaction.—With the exception of one, all reacting cases remained sensitive throughout the first experimental period of eight to twelve days. One (12) reacting positive on the seventh day, did not react after an intradermal given on the ninth day. Another (13) became positive on the ninth day, four days after the fourth intradermal, but refused to respond to a fifth intradermal given on this day. The refractory case (No. 2) reacted positive on the forty-first day. We have many instances in which sensitization, as recognized by the intradermal reaction, continues for many months. This is so whether the patient has received a large or a small initial dose of horse-serum. For example, Veronica H. received 1,000 units (6 to 7 c.c.) of antitoxin Oct. 30, 1912. She reacted to an intradermal injection November 27 and to another intradermal April 16, 167 days after first injection. Dec. 3, 1912, Velma C. received 2 cm.^{3} antitoxin intradermally for the first time, a second intradermal three days later, and on the following day a third intradermal. She reacted on the sixth day (probably on the fifth, as the reaction looked like a fading reaction, and no observation was made on the fifth). Later response was obtained at site of previous injection, showing that she was thoroughly sensitized. The maximum amount of horse-serum used was 4.5 cm.^{3} April 16, 134 days after the first injection, she reacted more vigorously than at any other time.

To return to our so-called refractory case, John C. (No. 2). This infant received his fifth intradermal injection on the ninth day. A neg-

ative result followed throughout the rest of the experimental period of thirteen days. With the exception of one (No. 7) all the other children reacted positive before this time. No. 7 was overlooked in making the injections on the ninth day and received his fifth intradermal on the tenth day. He had given a questionable reaction on the eighth day, but now reacted most vigorously. It is, of course, possible that John would have done the same had he received an injection on the tenth day. However, at no time did he show even a questionable reaction. On the forty-first day he received his sixth intradermal injection, which resulted in an entirely positive and typical reaction. Hamburger and Moro had a similar experience in which no oversensitiveness was demonstrable up to the twelfth day. They did not, however, make any tests later than this time. A very interesting question hinges on this point. We are referred back to the experiments of Rosenau and Anderson previously cited, which would argue that this infant was immune,[8] and to those of Gay and Southard, which showed that Rosenau and Anderson's animals were not really immune, but because of the large dose of serum they received were rendered insusceptible,[9] to become susceptible or sensitive at a later time. The experience encountered in my case would support the latter view and may be explained on these grounds. Just how far this hypothesis may be used to explain the peculiar light reactions in the children below 4 years of age referred to later is not at the present time easy to decide. The magnitude of the skin reaction seems to be in proportion to the degree of oversensitiveness.

Another interesting point bearing on this topic is the fact disclosed in experiments of Series 3. The four children here recorded received as their initial dose a very small amount of horse-serum. Specific oversensitiveness to an intradermal injection occurred after the same time interval necessary for the larger initial injection had elapsed. That is, the reaction occurred no sooner and no later than is the rule with the larger initial injection.

Local and General Character of the Reaction of the Organism.—In the beginning of work of this character a question arose as to whether

8. Indeed it is easy to determine that this infant, as well as all the others, received a comparatively much larger dose of horse serum than did the older children and the adult cases. Hence the concentration of the horse serum in these infants is analogous to that in the guinea-pigs of Rosenau and Anderson.

9. Besredka and Steinhardt apply the term anti-anaphylaxis to this phenomenon. See foot note 3.

these intracutaneous reactions were purely local in nature. The work on the cutaneous tuberculin test, on cow-pox vaccination and on serum sickness (Arthus, Hamburger, v. Pirquet and others), as well as my own observations, shows conclusively that the cutaneous reaction is an expression of a reaction of the entire organism. For example, all patients received their immunizing dose of antitoxin in the interscapular space. The intracutaneous tests were made at a remote point, arms and thighs. The location made no difference in the character or time of the reaction. Arthus determined this point by giving the primary injection intraperitoneally and Knoepfelmacher by excision of the developing vaccination lesion before it was full blown. A peculiar experience, however, was encountered in the susceptibility of some patients to reaction at the original site of inoculation, the interscapular space. Of the twenty-seven positive cases among the children, there were three (Nos. 8, 13, 17) which reacted in the interscapular space and one which showed a questionable reaction, not up to the threshold of cutaneous manifestation. Of the positive adult cases, nine reacted in the interscapular space (19, 20, 21, 22, 23, 25, 26, 27). The reaction at the site of the original injection was simultaneous or coincident with the appearance of the first positive intracutaneous reaction in nine cases (8, 15, 20, 21, 22, 23, 25, 26, 27). In others the reaction preceded or followed the appearance of the intracutaneous reaction.

From this experience it may be determined that the reaction at the site of primary injection is an expression of a high degree of oversensitiveness. With the exception of one, all cases responding in the back gave marked reactions on the arm.

Another interesting observation in this series is the response of previously negative areas to a renewed injection of serum (Fig. 1). By reference to the table it will be seen that frequently when a positive reaction occurs for the first time it does so at the point of the last intradermal injection (eight cases, 1, 3, 4, 5, 6, 7, 8, 11); in other cases all the previous points of injection react, and at times very markedly (Cases 7, 8, 10, 15, 16, 18, 19). Hamburger and Pollak regard these successive reactions as coreactions or focal reactions; that is, "They appear only through the provocative influence of reinjection and are similar to the negative tuberculin reaction which under the influence of tuberculin injections may become positive." In my adult cases, which received a second injection only after an interval of seven days had

No.	Name	Serum Originally Injected	Age Yrs	Day of Reaction to Intradermal Test*												
				1	2	3	4	5	6	7	8	9	10	11	12	13
1	Dean S....	5 c.c.	6/12	—	0	0	0	0	0	0	0	0	0	0	0	
		Concentration*‡		..	..	—	0	0	0	0	0	0	0	0	0	
				..	..	..	—	0	0	0	0	0	0	0	0	
				..	..	..	..	..	—	+	+	0	0	0	0	
		1-119		..	..	..	..	....	....	.....	.....	—	+	+	+	
2	John C....	5 c.c.	6/12	—	0	0	0	0	0	0	0	0	0	0	0	
		Concentration		..	..	—	0	0	0	0	0	0	0	0	0	
				..	..	..	—	0	0	0	0	0	0	0	0	
				..	..	..	..	....	—	0	0	0	0	0	0	
		1-85		..	..	..	..	....	....	.....	.....	—	0	0	0	
3	Zena B....	5 c.c.	8/12	—	0	0	0	0	0	0	0	0	0	0	0	
		Concentration		..	..	—	0	0	0	0	0	0	0	0	0	
				..	..	..	—	+?	+?	0	0	0	0	0	0	
				..	..	..	..	....	—	+	+	0	0	0	0	
		1-137		..	..	..	..	....	....	.....	.....	—	+	0	0	
4	Kate J....	5 c.c.	9/12	—	0	0	0	0	0	0	0	0	0	0	0	
		Concentration		..	..	—	0	0	0	0	0	0	0	0	0	
				..	..	..	—	+	+	0	0	0	0	0	0	
				..	..	..	..	....	—	+	+	0	0	0	0	
		1-76		..	..	..	..	....	....	.....	.....	—	+	0	0	
5	Melville....	5 c.c.	1½	—	0	0	0	0	0	0	0	0	0	0	0	
		Concentration		..	..	—	0	0	0	0	0	0	0	0	0	
				..	..	..	—	0	0	0	0	0	0	0	0	
				..	..	..	..	....	—	0	0	0	0	0	0	
		1-178		..	..	..	..	....	....	.....	.....	—	+	0	0	
6	Noel B....	5 c.c.	3½	—	0	0	0	0	0	0	0	0	+	0		
		Concentration		..	..	—	0	?	+	+	+	0	+	0		
				..	..	..	—	+	+	0	+	+	+	0		
				..	..	..	..	....	—	+	+	+	+	0		
		1-239		..	..	..	..	....	....	.....	.....	—	+	0		
8	Earl S....	5 c.c.	4	..	..	—	0	0	0	0	0	0	0	0	++	++
		Concentration		..	..	..	—	0	0	0	0	0	0	+	++	++
				..	..	..	..	....	—	0	0	0	0	+	++	++
		1 255		..	..	..	..	....	....	—	+?	0	0	+	++	++
				..	..	..	..	....	....	.....	.....	.....	—	+	++	+
8	Clifford....	5 c.c.	4	—	+	+	0	0	++	+	+	+	++	0		
		Concentration		..	..	—	+	++	++	+	++	+	++	0		
				..	..	..	—	++	++	++	++	+	++	0		
				..	..	..	..	....	—	++	++	+	++	0		
		1-255		..	..	..	..	....	....	.....	.....	—	++	+		
9	Harold S..	5 c.c.	5	—	0	0	+	0	0	0	0	0	0	0		
		Concentration		..	..	—	+	++	+	0	0	0	0	0		
				.	..	..	—	++	+	0	0	0	0	0		
				..	..	..	..	....	—	+	+	0	0	0		
		1-278		..	..	..	..	....	....	.....	.....	—	+	0		
10	Joe K..	5 c.c.	5	—	0	0	0	0	0	+	+	0	0	0		
		Concentration		..	..	—	0	0	0	++	+	0	0	0		
				..	..	..	—	0	0	++	+	0	0	0		
				..	..	..	..	....	—	++	++	0	0	0		
		1-278		..	..	..	..	....	....	.....	.....	—	+	0		

* Day after injection of antitoxin. — Intradermal injection. 0 Negative reaction. + Positive reaction.

† Day after injection on which reaction at original site of injection in the back occurred is marked +;

‡ The approximate concentration of the horse serum in the blood was calculated by regarding the total weight was taken for adults.

Day of Reaction at Original Site of Inoculation †												Remarks
1	2	3	4	5	6	7	8	9	10	11	12	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	
0	+	+	0	0	0	0	0	0	0	0	0	Second time patient has had antitoxin within ten weeks. Accelerated reaction marked.
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	0	0	0	0	0	0	

++ Very marked reaction.
negative reaction, 0.
quantity of blood as 1/13 of the body weight. When weights were missing the average was taken. A uniform

TABLE SHOWING THE SUCCESSIVE INTRADERMAL INJECTIONS

No.	Name	Serum Originally Injected	Age Yrs	Day of Reaction to Intradermal Test *												
				1	2	3	4	5	6	7	8	9	10	11	12	13
11	Ruth T....	5 c.c.	5	—	0	0	0	0	0	0	0					
		Concentration 1-278		..	..	—	0	0	++	0	0					
				..	..	..	—	+	++	0	0					
				..	..	..	..	....	—	++	++					
12	Lulu Q....	5 c.c.	6	—	0	0	0	0	0	0	0	0	0	0		
		Concentration 1-516		..	..	—	0	0	0	0	0	0	0	0		
				..	..	..	—	0	0	+	0	0	0	0		
				..	..	..	..	....	—	++	0	0	0	0		
				..	..	..	..	....	....	.....	.....	—	0	0		
13	Louise O...	5 c.c.	6	—	0	0	0	0	0	0	0	0	0	0		
		Concentration 1-516		..	..	—	0	0	0	0	0	+	0	0		
				..	..	..	—	0	0	0	0	+	0	0		
				..	..	..	..	—	0	0	0	+	0	0		
				..	..	..	..	....	....	.....	.....	—	0	0		
14	James H...	5 c.c.	7	—	0	0	0	0	0	+	0	0	0	0		
		Concentration 1-355		..	..	—	0	0	0	0	0	0	0	0		
				..	..	..	—	0	0	0	+	0	0	0		
				..	..	..	..	....	—	+	++	+	0	0		
				..	..	..	..	....	....	.....	.....	—	++	0		
15	Agnes B...	5 c.c.	9	—	0	0	0	0	0	++	++	+	0	0		
		Concentration 1-424		..	..	—	0	0	+	++	++	+	0	0		
				..	..	..	—	0	+	++	++	+	0	0		
				..	..	..	..	—	++	++	++	++	0	0		
				..	..	..	..	....	....	.....	.....	—	++	+		
16	Crystal B..	5 c.c.	11	—	0	0	0	0	+	++	+	+	0	+		
		Concentration 1-462		..	..	—	0	++	++	++	+	+	0	+		
				..	..	..	—	++	++	++	+	+	0	+		
				..	..	..	..	....	—	++	++	++	+	++		
				..	..	..	..	....	....	.....	.....	—	++	++		
17	Adrian W..	5 c.c.	13	..	—	0	0	+	0	0	0	0	0	0		
		Concentration 1-578		..	..	—	0	++	+	+	0	0	0	0		
				..	..	..	..	—	++	++	+	0	0	0		
				..	..	..	..	....	—	++	++	0	0	0		
				..	..	..	..	....	....	.....	.....	—	+	0		
18	Miss O.....	10 c.c.	21	..	—	0	0	+	++	++	+	0	++			
		Concentration 1-544		..	..	—	0	+	++	++	+	0	++			
				..	..	..	..	+	++	++	+	0	++			
				..	..	..	..	....	....	.....	.....	—	++			
19	Miss C.....	10 c.c.	21	..	—	0	0	+	+	0	0					
		Concentration 1-544		..	..	—	0	++	++	++	0					
				..	..	..	..	—	++	++	+					
				..	..	..	..	....	—	++	+					
				..	..	..	..	....	....							
20	Mrs. R....	5 c.c. Concentration 1-1088		..	..	..	..	....	....	—++	++++					

AND REACTIONS OF EXPERIMENTS, SERIES 1.—(Continued)

Day of Reaction at Original Site of Inoculation †												Remarks
1	2	3	4	5	6	7	8	9	10	11	12	
0	0	0	0	0	0	0	0	0	0	0	0	Left hospital ninth day.
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	+	0	0	0	0	0	Back shows an area 2.5 cm. in diameter at site of injection. There is also erythema over both knees, giving picture of serum sickness.
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	+	0	0	0	0	0	0	Back shows a slightly elevated and indurated area over site of injection 5 by 2 cm. in diameter. No signs of serum sickness.
0	0	0	0	0	0	0	0	0	0	0	0	
0	0	0	0	0	0	?	0	0	0	0	0	? Slight itching at site of injection in back, but no redness.
0	0	0	0	0	0	0	0	0	0	0	0	On the sixth day there were slight signs of serum sickness, but no reaction in the back.
0	0	0	0	0	+	0	0	0	0	0	0	On sixth day the back showed an irregular blotchy redness around site of injection 2.5 cm. in diameter.
0	0	0	0	0	0	S	0	0	0	0	0	On seventh day, before intradermal was given, a marked reaction occurred on back.

TABLE SHOWING THE SUCCESSIVE INTRADERMAL INJECTIONS

No.	Name	Serum Originally Injected	Age Yrs.	Day of Reaction to Intradermal Test *												
				1	2	3	4	5	6	7	8	9	10	11	12	13
21	Mrs. P.....	5 c.c. Concentration 1-1088		..	..	..	..	....	....	—+	++++					
22	Mrs. M....	5 c.c. Concentration 1-1088		..	..	..	..	...	....	—+	+++					
23	Mrs. B.....	5 c.c. Concentration 1-1088		..	..	..	..	...	....	—+	++					
24	Mrs. Pa....	5 c.c. Concentration 1-1088		..	..	..	..	...	....	—0	+++					
25	Mrs. Pal...	5 c.c. Concentration 1-1088		..	..	..	..	...	....	—+	++	+	0			
26	Mrs. T.....	5 c.c. Concentration 1-1088		..	..	..	..	...	....	—+	++	0				
27	Mrs. H.....	5 c.c. Concentration 1-1088		..	..	..	..	....	....	—+	++	+++	++++			
28	Mrs. W....	5 c.c. Concentration 1-1088		..	..	..	..	...	....	....	.....	—	++			
29	Mrs. Ha...	5 c.c. Concentration 1-1088		..	..	..	..	....	....	.....	.....	—	++	++		
30	Mrs. Wa..	5 c.c. Concentration 1-1088		..	..	0 —	..	....	....							

AND REACTIONS OF EXPERIMENTS, SERIES 1.—(Continued)

Day of Reaction at Original Site of Inoculation †												Remarks
1	2	3	4	5	6	7	8	9	10	11	12	
0	0	0	0	0	0	+	0	0	...	...	...	By slightly rubbing point in back redness occurs. Not so on opposite side.
0	0	0	0	0	+	+	...	...	...	...	...	Ten hours after intradermal marked reaction in back.
0	0	0	0	0	0	++	+	...	...	...	...	Ten hours after intradermal marked reaction in back.
...	...	...	...	...	...	.....	...	...	...	...	...	No observation of back made.
0	0	0	0	0	0	0	+	...	...	...	..	Slight flush over point of injection in back on eighth day.
0	0	0	0	0	0	0	+	...	...	..	...	Diffuse urticarial eruption over site of injection in back.
0	0	0	0	0	0	0	+	+	...	...	...	Ten hours after intradermal marked reaction in back.
...	...	...	...	...	...	.....	...	...	...	...	...	No observation of back made.
...	...	...	...	S	S	.....	...	...	...	..	...	On fifth day, before intradermal was given, reaction occurred on back; no other signs of sickness.
...	...	...	...	...	...	.....	...	...	...	...	...	No observation of back.

elapsed, this provocative influence of successive injections is removed. The marked reaction in the back in all these cases is an expression of a general reaction of high degree, brought about by the primary injection. It probably would not have occurred without the provocative influence of the small intradermal injection. However, one case (No. 20) illustrates the fact that a marked reaction may take place without the provocative influence of a second injection. It will be further observed that in all children below the age of 4 years (five observations) no marked reactions took place, while after this age and apparently as the age increases up to adult life, the reaction becomes stronger. This cannot be because of a greater amount of serum administered with the initial injection for just as large doses were given to children with the exception of two (18, 19) as were given to adults. Even in these cases, if we figure the concentration of the serum in the blood the children received in proportion to the total quantity of blood in the body by far the greater doses. The explanation would seem to rest either with the experience encountered with animals, namely, that a small sensitizing dose gives rise to a greater sensitization and that the adult cases are analogous to this because of the higher dilution of the original injection, or with the theory that the reaction power of the body has become greater and quicker as age has advanced. The observations are so few that they merely suggest this latter explanation. At this point we must recall the fact previously referred to, that while a small dose may give greater sensitiveness in animal experiments, the symptoms of serum disease are usually induced only by large doses of serum (particularly where the symptoms follow a primary injection). We must also ask the question, Is the cutaneous reaction analogous to or identical with the symptoms of serum disease? This question will be discussed later (Series 2).

Character of the Cutaneous Reaction.—If a well-marked reaction is closely observed it will present two distinct zones, an inner, slightly raised anemic zone of infiltration and an outer flat zone of hyperemia, the periphery of which has finely jagged edges. Less marked reactions present only a flat hyperemia, a mottled roseolar, measles-like eruption or a group of small wheals. At times well-marked local urticaria accompanies a pronounced reaction. In my experience tenderness was seldom complained of or induced by pressure. Itching was a frequent symptom. It was more marked in the adult cases, Series 2, and the reinjection Case 8, and at times it was almost intolerable.

If the progress of a well-marked lesion is observed the total area will be seen to increase markedly from day to day until it has reached its height, after which it may persist a day and then disappear. At times a yellowish or greenish-yellow stain remains for a short time. If one computes the total area on successive days and plots a curve, the curve will follow closely that of a geometric progression. Nearly all reactions were measured daily in their longitudinal and transverse dimensions. It is not possible from such measurements to determine the total area with any degree of accuracy. This point is considered more in detail in "Studies on the Incubation Period No. 2—Cow-Pox Disease."[10] V. Pirquet and Hamburger and Schey have called attention to its significance.

The Effect of Gentle Rubbing.—I have frequently observed in a number of reactions, which were subsequently positive, that a day before the lesion became definitely positive gentle brushing over the injected area with the finger brings about a blush not produced by similarly rubbing some remote part of the body. I have also observed that in some cases in which the reaction might otherwise be questionable, this brushing brings it to the surface in such a way as to convince one of its positive nature. It might be interpreted that such a reaction was just below the threshold of cutaneous manifestation.

SERIES 2

Observations to Determine How Long an Individual Remains Sensitive to an Inoculation of Horse Serum, and the Factors Influencing the Reaction.

We have recorded already many instances of sensitization continuing for one year. The following cases record observations beyond this period:

CASE 31.—Miss S. was given antitoxin for the first time seventeen months ago.

April 18.—Intradermal in left forearm 0.5 cm.^{3} diphtheria antitoxin. In fifteen minutes an area of erythema and urticaria about 30 by 30 cm. appeared. At night this area began to itch.

April 19.—There is a marked area 125 by 60 mm. The itching is very marked. Infiltration not noted.

April 20.—The area has entirely disappeared.

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10. Read at meeting of American Society for Advanced Clinical Investigation, Washington, May 5, 1913. Unpublished.

CASE 32.—Miss A. was given diphtheria antitoxin for the first time two years ago. No serum sickness occurred.

April 18.—Intradermal left forearm 0.5 cm.³ Immediate reaction of same degree as Case 31. Itching at night marked.

April 19.—There is a marked reaction. The central portion 40 by 35 mm. is infiltrated. The outer area 120 by 70 mm. is red. Itching is marked. There is a large urticarial lesion over the left wrist 40 by 40 mm.

April 20.—The reaction has disappeared. Patient was very uncomfortable during the exanthem.

CASE 33.—Miss K. was given diphtheria antitoxin for the first time seven years ago.

April 18.—Intradermal 0.5 cm.³ diphtheria antitoxin. An immediate reaction occurred within fifteen minutes.

April 19.—Patient complained of marked itching of the forearm last night. This morning there is an inner zone of infiltration 80 by 60 mm. and an outer zone of erythema 110 by 90 mm. The entire forearm is swollen.

April 19.—The arm is almost entirely clear.

April 20.—The arm is clear.

April 23.—Last evening a large area began again in the same location as before. This morning it covers the entire flexor surface of the arm and extends well around to back of arm. The itching last night was intense. There is none this morning. Other parts of the body have been free from eruption.

From these observations we find that an individual may remain very markedly oversensitive (allergic) for seven years. This is the longest definite case without reinjection, I have been able to find. To repeat, this remarkably robust woman reacted immediately, within fifteen minutes, with erythema. During the following night she was annoyed by marked itching of the arm and at the end of twenty-four hours a zone of marked infiltration 60 by 80 millimeters surrounded by an outer zone of erythema 90 by 100 millimeters had developed. The entire forearm was swollen (immediate reaction). The following day the hyperemia had almost entirely disappeared. Four days later, however, intense itching, erythema, urticaria and infiltration covered the entire flexor surface of the forearm (hastened reaction and double reaction). This brings us to the consideration of the immediate, hastened and double reaction of von Pirquet and Schick.

In certain cases after reinjection with horse-serum, v. Pirquet and Schick observed that when the reinjection was made early, within two to four weeks after the primary injection, if the symptoms of serum sickness appeared at all, they usually did so within the first twenty-four hours. If an interval of six months intervened the symptoms appeared only after several days, but in advance of those that occur after a primary injection. The first they called the *immediate reaction,* the second the

hastened reaction. They made a still further observation, that in certain other cases after reinjection both of these reactions may be observed; that is, symptoms appear within twenty-four hours, then disappear and reappear after an interval of three or four days. This they called the *double reaction.* It is not infrequently seen in cases of serum sickness, and it is beautifully illustrated in the local reaction in the case of Miss K. (No. 3).

The immediate intradermal reaction is the rule in individuals who have passed the pre-allergic stage (four to ten days), and the experience encountered with the intradermal reaction, while not identical with, is analogous to, that of serum sickness proper. The difference between the two seems to be only in the fact that with the intradermal test an immediate reaction is always obtained whether the reinjection is made during the first few weeks of allergy or after the six-month interval, up to the seventh year.

In answer to the question raised before, Is the cutaneous reaction analogous to or identical with the symptoms of serum sickness, it may be said that they are one and the same thing, the difference being a quantitative one. Diluted serum, as Hamburger and Pollak have shown, brings about a fainter reaction than undiluted, and clinical experience shows us that 2,000-unit reinjection is much more likely to bring about the symptoms of serum disease than a 500-unit reinjection.

SERIES 3

Observations to Determine if a Small Dose of Horse Serum Is Sufficient to Sensitize to the Point of Recognition by the Intradermal Test and if so for How Long.

CASE 34.—Louise C. Little's disease. Has never had antitoxin.

Nov. 29. Was given 1 cm.³ antitoxin intradermally in the right arm and 1.5 cm.³ subcutaneously.

Day 1—Nov. 30. Arm negative.
Day 3—Dec. 2. Negative.
Day 4—Dec. 3. Negative; 2 intradermal 2 cm.³ same arm.
Day 5—Dec. 4. There is a very slight reaction, 5 mm. diameter, which is increased to 10 mm. by gentle rubbing. Rubbing over other sites of injection gives same redness.
Day 7—Dec. 6. Faint area 20 mm. in diameter, fading.
Day 8—Dec. 7. All negative.

Total serum given, 4.5 cm.³

Case 35.—Lillian O. Same as patient in Experiment 2, Series 4. Has never had antitoxin.

Nov. 29. Was given first injection 1 cm.³ antitoxin intradermally and 1.5 cm.³ subcutaneously. There was no reaction after

three days when she was given a second intradermal of 2 cm.³ She was sensitive on the following morning. Fourth day, area 30 by 30 mm. with indurated center. See further records Series 2.
Total amount of serum given, 4.5 cm.³

CASE 36.—Velma C. Patient has never had antitoxin.
1—Dec. 3 was given 2 cm.³ antitoxin intradermally and 2 cm.³ subcutaneously, right arm.
Day 1—Dec. 4. Red trauma-like area 5 mm. in diameter.
Day 3—Dec. 6. Negative; 2 intradermal 2 cm.³ in left arm.
Day 4—Dec. 7. Negative; 3 intradermal, 1 cm.³ in right arm; 4 intradermal 1 cm.³ in right thigh.
Day 6—Dec. 9. Faint area 25 mm. in diameter at point of third injection, fading. Thigh negative. No observation on fifth.
Day 7—Dec. 10. Left arm shows faint area of mottled hyperemia 25 by 25 mm. Right arm 30 by 30 mm., faint but distinct hyperemia. Right thigh negative.
Day 8—Dec. 11. Right arm 60 by 35 mm., light pink erythema. Left arm same as yesterday. Right thigh negative.
Day 135—April 18. Fifth intradermal 0.5 cm.³ At 7 p. m. area 15 mm. in diameter (approx.)
Day 136—Apr. 19. Area of pink mottling 30 by 60 mm.
Total serum previous to last intradermal 8 cm.³ (8/10 c.c.)

CASE 37.—Minnie A. Patient has never had antitoxin.
Nov. 27. Was given 2 cm.³ antitoxin intradermally in arm.
Day 1—Nov. 28. Slight hyperemia 0.5 cm.³ in diameter (trauma) increased by gentle rubbing.
Day 2—Nov. 29. Faint area as before. Rubbing does not excite it.
Day 3—Dec. 2. Negative.
Day 4—Dec. 3. Negative. Second intradermal 0.5 cm.³
Day 5—Dec. 4. Point of second injection shows an area of slight erythema with indurated center 30 by 30 mm.
Day 7—Dec. 6. Deep red erythema 40 by 30 mm. Distinctly indurated. No tenderness.
Day 8—Dec. 7. Erythema same as yesterday.
Day 10—Dec. 9. Area same size but fading.
Day 12—Dec. 11. Area fading but visible 30 by 30 mm.
Total amount of serum given 2.5 cm.³ (¼ c.c.)

From these observations we find first, that typical oversensitiveness as recognized by the intradermal test is brought about in a child by at least 1 cubic millimeter of horse-serum (1/10 c.c.) without the provocative influence of successive injections (Case 35), and that the reaction continued over a period of seven days; second, that the reaction occurred in all cases on the fourth or fifth day, as is the rule after the longer initial injection (5 to 10 c.c.); third, that the reaction is qually as pronounced as it is after the larger injection at the same period of observation (Case 37); and fourth, that sensitization by means of a minute

dose of horse-serum continues for 136 days (Case 36, longest observation made).[11] As the point sought in these observations was only to determine if a very small dose of horse-serum would bring about sensitization, as recognized by a skin reaction, and the duration of the sensitization, further tests to determine the time at which the maximum reaction would take place were not made. In one case (36) a test was given on the one hundred and thirty-fifth day, and an immediate reaction developed within nine hours and became marked by the end of twenty-four hours. This reaction was much more marked than the first one, and shows that at the time of the first reaction sensitization had not reached its height.

SERIES 4

Does Horse Serum Exist as Such in the Circulating Blood and if so for How Long.

It will be recalled that previous reference has been made to this question. Hamburger and Moro, by means of the anti-horse-serum method, were able to show that horse-serum or what has been thought to be its biologically active portion (precipitable substance) continued in the blood-stream apparently unaltered as long as thirty-one days after injection, and that precipitable substance and precipitin exist side by side for a long time. By an entirely different method I have attempted to demonstrate the same point. Instead of using the body of a foreign species to bring about an antiserum I assumed that the organism of a highly sensitized individual should respond to an intradermal or subcutaneous injection of the blood-serum of an individual recently injected with horse-serum for the first time, if the horse-serum continued as such in the body (provided that the dilution of the serum was not too high). In other words, the serum of an unsensitized injected child if injected into a highly sensitized child would bring about either an intradermal reaction or the symptoms of serum disease in the sensitized child. On the convenient hypothesis of v. Pirquet and Schick, *allergen* and *ergin* are necessary for a reaction. These conditions are supplied in this experiment.

11. A patient with a mild attack of diphtheria was given within thirty-six hours approximately 20 c.c. of antitoxin. Intradermal tests on the fourth and sixth days were negative. The case then passed from observation. This apparently prolonged preallergic stage suggests the anti-anaphylactic reaction of Steinhart and Besredka.

Sensitized Child.—By reference to Case 8, Series 1, it will be seen that Clifford H. had a very high degree of oversensitiveness to horse-serum. In other words, *allergy* had been established and *free ergin* was present in the circulation.

Unsensitized Injected Child.—For this purpose I sought a perfectly healthy, tuberculin-negative child, Theo. H., who in consequence of prophylaxis received Dec. 21, 1912, 1,000 units diphtheria antitoxin (5 c.c.). [illegible] twenty-four hours 2 c.c. of blood were taken from an arm vein, the serum separated and marked 1. On the following day a similar sample was taken and marked 2 (forty-eight hours). On the third day another sample was taken and marked 3 (seventy-two hours). The serum was obtained by coagulation and was preserved in an ice-chest.

Experiment 1.—Clifford H. (Case 8, Series 1). A highly sensitized patient was injected:

Dec. 21.—11 a. m. with 0.5 c.c. serum No. 1 intradermally in the arm.

12 m. There is a distinct hyperemic area at the site of puncture 2 by 1 mm.

2 p. m. The hyperemic area is very much diminished and limited to a very small areola about the puncture. (Observation by Dr. Stoops.)

3:30 p. m. The area remains about the same.

6:30 p. m. The area is again visible 1 by 1.5 mm. surrounding the puncture. The pale center observed at noon has disappeared. (Stoops.)

8:30 p. m. (D. M. C.) The area over the arm has faded. At 7 p. m. the nurse records that the patient complained of headache. At 8 o'clock she records slight redness over the forehead, temple and chin. At present there are several deep red hyperemic areas with irregular borders over the face and forehead, varying from 10 by 30 mm. on the forehead. No urticaria. There is a large hyperemic area over the back of both wrists. Back and rest of body negative. These are not pressure spots as the patient has been sleeping on the opposite side. T. P. R. normal.

Dec. 22—11 a. m. There is a faint hyperemic area 7 by 5 mm. around the point of injection in arm. The spots on the face have almost completely disappeared.

Dec. 23—10 a. m.—One cm.^{3} Theo. serum No. 1 intradermally, right arm. A pink hyperemia developed immediately. One cm.^{3} of sterile water is similarly injected in left arm. After ten minutes the area on the right arm is reduced 3 by 5 mm. and an area 4 by 2 mm. develops in five minutes after the injection of water.

10:35 a. m. R. A. (water), 5 by 2 mm. L. A. (serum), 4 by 2 mm.

11:30 a. m. R. A. (water), 2 by 1.5. L. A. (serum), negative.

12:00 a. m. R. A. (water), negative. L. A. (serum), negative.

11:00 p. m. Nurse records slight redness on left side of neck and upper part of shoulder.

Dec. 24—6:00 a. m. Slight redness on cheek.

11:30 a. m. Slight but distinct blotchy redness about the mouth and on right side of nose. Left arm shows an area of hyperemia 7 by 5 mm. around site of puncture with slight induration. Control on other arm is entirely negative.

11:45 a. m. Intradermal 1.5 cm.^{3} Theo. serum No. 3 (seventy-two hours).

12:00 a. m. There is marked area 30 by 15 mm. with white center.

From this experiment we may conclude that horse-serum or its biologically active portion, *allergen,* was present in the blood-stream as late as forty-eight hours after injection, possibly seventy-two hours. It is of interest to note that the local reaction was not so marked as the general reaction.

To see if a similar result would occur in a child sensitized with a very small dose of horse-serum, I made a similar observation on a child previously successfully sensitized with 0.1 c.c. horse-serum as follows:

Experiment 2.—Lillian O. (Case 35, Series 3.) Patient has never had antitoxin.

Nov. 29, 1912. Patient was given 1 cm.³ diphtheria antitoxin intradermally and 1.5 cm.³ sucutaneously to see if this small amount would produce sensitization.

Day 1—Nov. 30. Arm and back negative.

Day 3—Dec. 2. Arm and back negative.

Day 4—Dec. 3. Arm and back negative; 2 intradermal 1 cm.³

Day 5—Dec. 4. Characteristic hyperemia with indurated center. Back negative.

Day 7—Dec. 6. There is a deep hyperemia 10 by 9 mm., both points fusing. There is considerable induration, same as yesterday.

Day 8—Dec. 7. Same as yesterday, possibly fading a little.

Day 10—Dec. 9. Fading.

Day 11—Dec. 10. Reaction still present but less noticeable.

Day 12—Dec. 11. The area is still visible 10 by 9 mm., fading.

Day 22—Dec. 21. Patient is given an intradermal of about 1 cm.³ of Theo. serum No. 1. In half an hour there is no change. The area of injection is still elevated. (Primary infiltration.) 8:30 p. m., the arm shows an area of slight hyperemia 10 mm. in diameter. There is a large hyperemic area 50 by 50 mm. over the right inner forearm above the wrist of a deep red color similar to Case 1. This area has irregular map-like margins. There is also a slight diffuse redness of the left wrist. The rest of the body is free. T. P. R. normal. 10 p. m. nurse records redness on back right hand.

Day 23—Dec. 22. 11:00 a. m. There is a slight but distinct hyperemic area 2 by 1.5 mm. at site of intradermal injection. The erythematous spots of last night have distinctly disappeared. On gentle rubbing over the intradermal area it is very much increased and mottled in character.

Day 24—Dec. 23. 10:30 a. m. Patient is given 0.5 cm.³ Theo. Serum No. 2 intradermally. Quite a little oozed from puncture. Fairly good infiltration obtained. No immediate reaction. 10:35 a. m. There is a hyperemic area 3.5 by 3.5 mm. with raised center and an outer zone 8 by 8 mm. The center in indurated. 11:35 a. m. The center in indurated as before; otherwise negative. 4:30 p. m. Area 4 by 4 mm. 7:00 p. m. Area negative. (Stoops.) 12:00 midnight, negative.

Day 25—Dec. 24. Nurse recorded no skin changes during the night. Point of intradermal shows a faint but distinct area of hyperemia 15 by 10 mm. This brightens up markedly on gentle rubbing. Other areas on arm do not.

Note.—This patient had been getting 18 drops of tincture belladonna t. i. d. for some days. She had never shown any hyperemia before and has shown none since injections have ceased. The evening both these cases reacted I made the rounds of both wards to see if any other children had areas of hyperemia. They were all negative.

In this case we found an even more marked reaction than was obtained in Experiment 1. In ten hours there were distinct signs of serum disease, with local reaction following the injection of both samples of Theo.'s serum. Theo. left the hospital at this point, so that further observations could not be made. Another opportunity did not present itself. From these two experiments it would seem that by a more carefully planned experiment an intradermal reaction might be obtained by this method at least up to the end of the fifth day of the incubation period, possibly later.

In the absence of such an experiment we must at this point consider the work of Gay and Southard on guinea-pigs and its possible bearing on the question in hand. These authors have demonstrated quite conclusively that the sensitizing substance of horse-serum continues in the animal body indefinitely [after the disappearance of precipitable substance], and confirm the observation first made by Rosenau and Anderson that it is transmitted to the offspring of sensitized guinea-pigs, and that when the serum from such an animal is injected into a non-sensitized guinea-pig it renders the pig sensitive. There are no observations that I am aware of which show that the serum of a sensitized pig or individual will induce a skin reaction in another sensitized animal of the same species.

I am unable to find record of any experiments similar to those just recorded. If by future work such reactions can be demonstrated to occur with any regularity, it would seem that a new and profitable field for research in the exanthematous diseases is opened up. It was this idea which prompted these experiments. For such a study one must have at hand incubating cases, recently recovered cases and cases representing weeks, months and years post-measles, scarlet fever, etc. In my first-attempted series in which it seemed that a most fortunate opportunity presented itself the unexpected happened. One child in a family of four children came down with a marked attack of morbilli. The

other children were fully exposed. Blood taken after a number of days reacted negative. These children, however, failed to contract the disease, accordingly only negative results would happen. There are many phenomena occurring in the exanthematous diseases which can be explained on the grounds of allergy. These must necessarily occupy our attention in the future, for as yet they are not fully understood and are but seldom recognized.

From this study I believe it is shown that the incubation period in serum disease is divided into three distinct stages, which for convenience I have designated pre-allergic, allergic and hyperallergic.

The Pre-Allergic Stage.—Directly following the injection of *allergen* there elapses a period of hours or days before it effects an altered state, "a changed reactivity," of the organism. The length of this stage cannot be definitely determined. For the present it may be considered to continue up to the day when a cutaneous reaction is demonstrable. Evidence has been brought forth to show that a binding of the reaction products has taken place before this time. When the binding begins we do not definitely know. This pre-allergic stage, as designated, differs with the allergen. With horse-serum it is four to five days. With cow-pox vaccine it is only twenty-fours or less. With tuberculin it is several days. In all probability during this stage the foreign serum is split into its component parts.

The Allergic Stage.—Following the time when a cutaneous reaction is demonstrable, there is a period of four or five days before the height of a cutaneous reaction is reached, and before the symptoms of serum disease spontaneously show themselves, and during which *ergin* is being elaborated in progressively larger amounts, but the reaction is still below the "threshold of cutaneous manifestation."

The Hyperallergic Stage.—Those individuals who respond to an injection of *allergen* with characteristc symptoms of the disease have passed into the hyperallergic stage. *Ergin* has now reached its highest point. Hereafter, depending on the degree of allergy or hyperallergy, the individual if again given an injection of *allergen* no longer passes through a pre-allergic stage, but either passes directly into hyperallergy (immediate reaction) or hastens through the allergic stage reacting with characteristic symptoms three or four days ahead of a primary injection case. Furthermore, those individuals who have never progressed to the hyperallergic stage remain allergic and likewise deduct the pre-allergic stage from their new so-called incubation period.

These phenomena are well illustrated by the curves in Chart 1. Curve C (Fig. 2) represents a case of serum sickness following a first injection. This curve represents a geometric progression with the *term* 1, and a *ratio* of 2. It reaches the threshold of biochemic demonstration the middle of the fifth day and that of cutaneous or clinical manifestation on the eighth day. Thereafter the reaction products are present in the body. If we regard the amount of reaction bodies retained in the body as represented by the *term* 5, and after a proper lapse of time give a second injection of the same amount of *allergen* as that given at

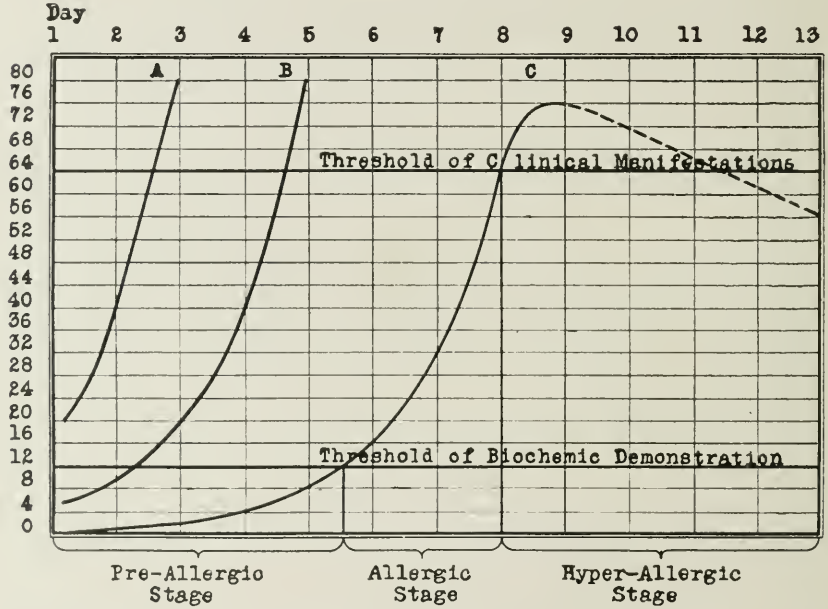

Fig. 2.—Chart showing curves of allergic reaction in serum disease. A, immediate reaction; B, hastened reaction; C, primary reaction.

the primary injection, we may again regard the *ratio* as 2 and we will produce a curve, B (Fig. 2), which exactly corresponds to a hastened reaction. If more *ergin* has been left in the body and an immediate reaction takes place on reinjection, it must correspond to a *term* of 20 if the *ratio* remains the same. Plotting such a curve gives the picture of an immediate reaction, A (Fig. 2), the cutaneous test appearing within the first twenty-four hours, the symptoms of serum disease the following day.

Von Pirquet and Schick, as well as others, were of the opinion that the reaction bodies entered the circulation suddenly after eight or ten days had elapsed. Experience with the cutaneous reaction introduced by Hamburger and Pollak tends to alter one's opinion on this point. It leads one to believe that the antibodies enter the circulation suddenly at a much earlier time, on the fourth or fifth day, and multiply with great rapidity from then on until they reach their height on the eighth to the tenth day, at which time they may manifest themselves in the visible symptoms of serum disease. However, we are forced to conclude that the

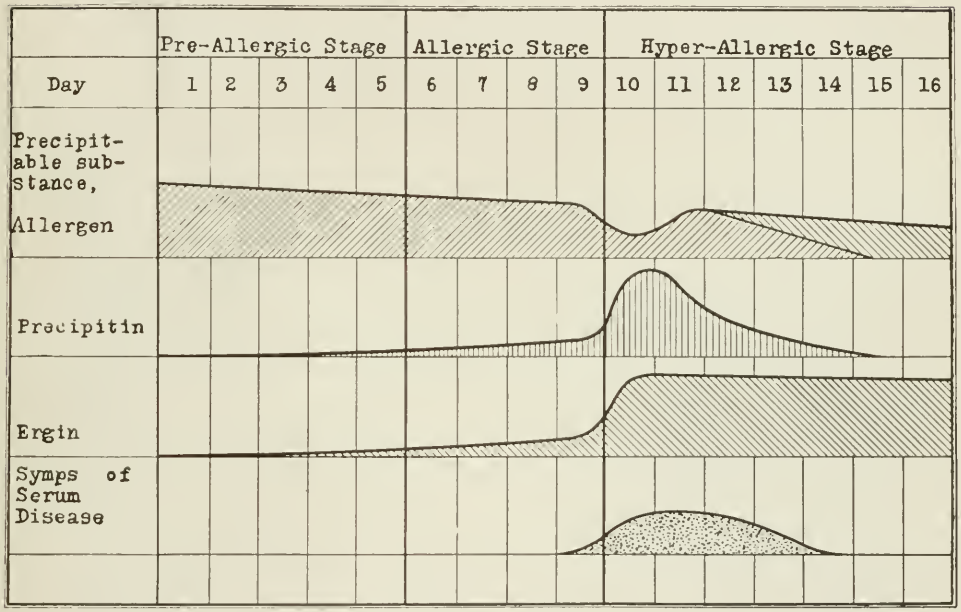

Fig. 3.—Curves illustrating phenomena during the three stages of the incubation period.

antibodies (reaction products) multiplying according to the law of geometric progression, must necessarily at first enter the circulation gradually after a primary injection of *allergen*. Evidence tends to show that these products are first bound, then enter the general circulation and multiply with great rapidity.

Figure 3 illustrates the phenomena observed during the three stages of the incubation period. Precipitins for horse-serum and *ergin* are

demonstrable at about the same time, that is, in the allergic stage. They gradually increase until about the ninth day, after which they increase with marked rapidity (hyperallergic stage). Precipitable substance is demonstrable during all three stages, but evidence tends to show that it decreases with the marked increase in the other two bodies during the hyperallergic. Precipitin and precipitable substance disappear at approximately the same time, but the other substance, *ergin,* continues in the blood indefinitely. This substance is not identical with precipitable substance or precipitin. In animal experiments it has been proved that a substance capable of acting the part of *allergen* remains in the body for a long time; that is, blood-serum from such an animal may be used to sensitize an unsensitized animal. This substance has been called *anaphylactin* by Gay and Southard. As it is derived from or is part of the original horse-serum (*allergen*) I have represented it on the chart by reverse hatching following the disappearance of precipitable substance.

It has been thought by some that the portion of horse-serum recognized by the precipitin test (precipitable substance) is the *allergin.* The early work of Rosenau and Anderson shows that this is not so. When they injected sensitized animals with filtrate of normal horse-serum, resulting from the precipitation of precipitable substance by antiserum, it was found to be toxic (2 c.c. caused death in twenty minutes). Several questions arise at this point. Is the substance present in the filtrate the original *allergen* which induces the cutaneous reaction? Is precipitable substance capable of inducing allergy as recognized by the cutaneous reaction? What part if any does precipitin play in the mechanism of allergy? Future experiments will have to give the answer. We must conclude at least that up to the present time the long-discussed question of the relation of precipitin and precipitable substance to anaphylaxis and the cutaneous manifestations of serum disease remains unsettled.

CONCLUSIONS

1. The so-called incubation period of serum disease passes through three distinct stages, which may be designated pre-allergic, allergic and hyperallergic, depending on the degree of reaction of the organism as a whole, all of which can be definitely determined.

2. The duration of the pre-allergic stage is uninfluenced by the smallness of the dose of serum.

3. The visible symptoms of serum disease are due to hyperallergy.

4. The hastened and immediate reactions depend on quantitative reaction factors.

5. The blood-serum of a normal child recently injected with horse serum, for the first time, when injected in small amount into a highly allergic child will induce the symptoms of serum disease as recognized by an immediate or a hastened reaction.

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MUCOUS CYST OF THE CECUM IN AN INFANT TEN WEEKS OLD, PRODUCING OBSTRUCTION OF THE ILEO-CECAL VALVE AND SYMPTOMS SIMULATING AN INTUSSUSCEPTION

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For the privilege of reporting this very interesting case I am indebted to the courtesy of my confrères in the Montreal General Hospital, Drs. J. M. Elder and A. H. Gordon.

History.—Chas. H., aged 10 weeks, was first seen in consultation by Dr. Gordon March 9, 1913, for continued vomiting. The infant had been nursed by its mother and had thriven well for the first two months of life. Then it began to vomit after taking nourishment. The physician who first saw it regarded the mother's milk as the cause of the trouble and advised artificial feeding. This was tried without benefit; the vomiting persisted and the nutrition failed rapidly. There was no pyrexia. When Dr. Gordon saw it in consultation he recognized a sausage-shaped tumor in the left lower right quadrant of the abdomen and recommended immediate operation. It was at once brought to the Montreal General Hospital and placed under the surgical service of Dr. Elder.

Examination.—The notes on entrance are as follows "Infant, 10 weeks old, well developed for age; nutrition poor; very little subcutaneous tissue; no glandular enlargements; lungs and heart normal; abdomen distended. In the right lower quadrant is a sausage-shaped tumor, distinctly palpable, 3 inches long by about 1 inch in diameter, freely movable, not tender; no muscular rigidity of abdominal walls. Distinct peristaltic waves are noticed traveling toward the site of tumor. Temperature 99, pulse 140, respirations 40."

Treatment and Course.—Shortly after entrance into the ward a high enema was given which brought away no flatus, and only a small amount of feces, in which there was no appearance of blood or much mucus. Following this the abdomen was immediately opened by Dr. Elder under spinal anesthesia. The oblong tumor mass was found to involve the lower portion of the ileum and cecum; above the mass the ileum was much distended, while below it the ascending colon was collapsed. Regarding it at first as an ileocecal intussusception, careful efforts were made at reduction, and when they failed, a resection was performed with end to end anastomosis, and the abdomen closed. On examination afterward of the incised mass its true nature was disclosed.

The child had no symptoms of shock after operation and for several days its condition was good. On the third day the temperature fell to normal, the abdomen was soft, the bowels moved freely and the infant was placed under my charge for its feeding. On the tenth day after the operation, however, the pulse became weaker, the face assumed an earthy hue, the features became drawn, and on the morning of March 24, twelve days after the operation, death occurred from peritonitis.

Pathologist's Report.—The pathological report on the specimens removed at operation was as follows: "The tumor consists of the lower portion of the cecum with its contained cyst, and the appendix. The cyst, much collapsed, measures about 2 cm. in diameter, is unilocular, contains glairy mucoid material and is situated on the wall of the cecum opposite the ileocecal valve, extending over to and completely obstructing that orifice."

Microscopical Examination.—Microscopic examination of the cyst walls showed the surface of the tumor projecting into the lumen of the cecum to be covered with mucous membrane similar to that of the intestine; the cyst to be lined with a somewhat stretched layer of columnar epithelium which, however, in some places was folded into gland formations. Beneath each surface of epithelium was a submucosa infiltrated with lymphocytes, and between these again are three more or less distinct layers of muscle.

Diagnosis.—From this report the cyst was regarded as in all probability a retention cyst, arising either from some fault in development or from an inflammatory occlusion of the mouth of the original gland.

Retention cysts of the appendix are not very uncommon and many cases have been reported during the past few years by various writers, but after a careful search of the literature I have been able to find no instance of a retention cyst of the cecum exactly similar to the one I am reporting. Harrington Sainsbury,[1] reports the case of a cystic tumor of the cecum met with in a girl of 11 years who died from an attack of typhoid fever. At the post mortem a large, soft, fluctuating tumor, about the size of a duck's egg, was found occupying the cecum and distending slightly the gut. It arose from the anterior wall just above the level of the entry of the ileum. On opening the tumor it was found to be a cyst filled with dark, ropy, mucoid fluid. Under the microscope the outer layer was seen to be mucous membrane similar to that lining the large intestine. The inner layer was much thinned and appeared to resemble a serous membrane, but the writer qualifies this in a foot-note by adding that the epithelial lining of such a cyst was probably mucous in character, but would be much modified by the distention and its appearance still further altered by death. In all probability, he says, it was a retention cyst and further adds that he knew of no similar case, and those whom he consulted were unable to give any reference to cases of like nature.

A. Krogius[2] reports a case of an intestinal cyst in a child 2 months of age, giving rise to obstruction and intussusception. The abdomen was opened and a resection of the gut with formation of an artificial anus was made. Death took place from hemorrhage. The cyst, which had

1. Sainsbury, Harrington: Trans. Path. Soc., London, 1887, xxxviii, 146.
2. Krogius, A.: Ztschr. f. klin. Med., 1903, xlix. 53.

the character of a retention cyst, was of the size of a pigeon's egg and was situated in the ileum close to the valve.

In his paper, Krogius refers to four previous cases, in which a cyst in the intestinal wall encroached on the lumen of the gut and produced symptoms of obstruction.

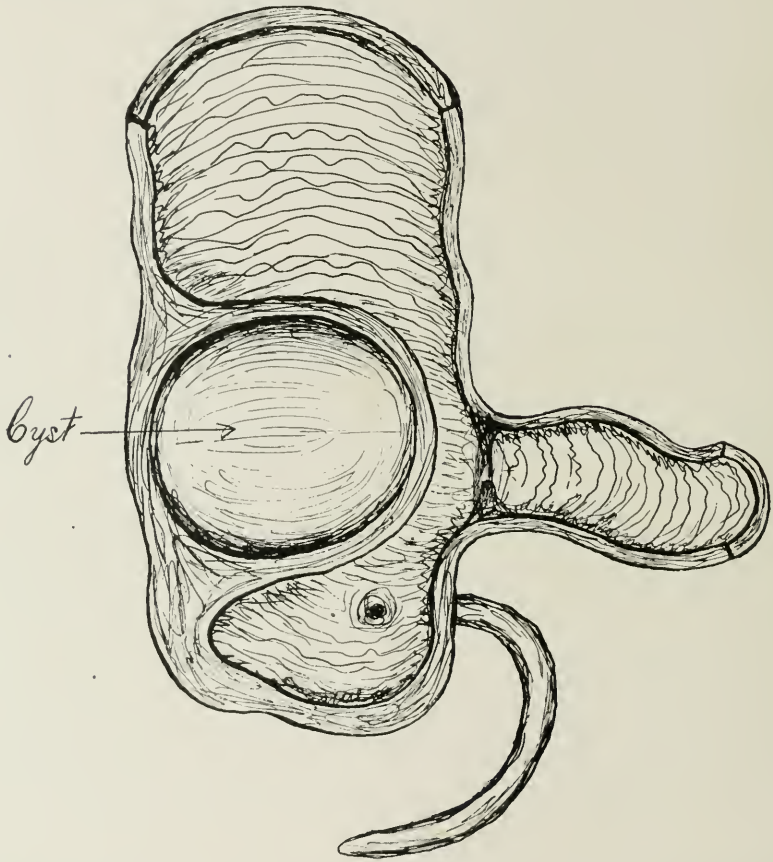

Fig. 1.—Diagram to represent cecum, ileum and cyst cut longitudinally.

The first case which he quotes was observed by E. Fraenkel[3] in 1851. An infant, a few days old, developed suddenly symptoms of obstruction of the bowels and died. The autopsy revealed as the cause of the obstruc-

3. Fraenkel, E.: Virchow's Arch. f. path. Anat., 1882, lxxxvii, 275.

tion a cyst 2.5 cm. in diameter close to the ileocecal valve; this appears to have had the characters of a retention cyst.

The second case was noted by Kulenkampff[4] in a 3-year-old boy, in whom, suddenly after a dose of calomel, given for obscure symptoms of obstruction, violent vomiting set in followed by collapse and death. A cyst in the mesentery compressing the ileum appeared to be the cause of obstruction.

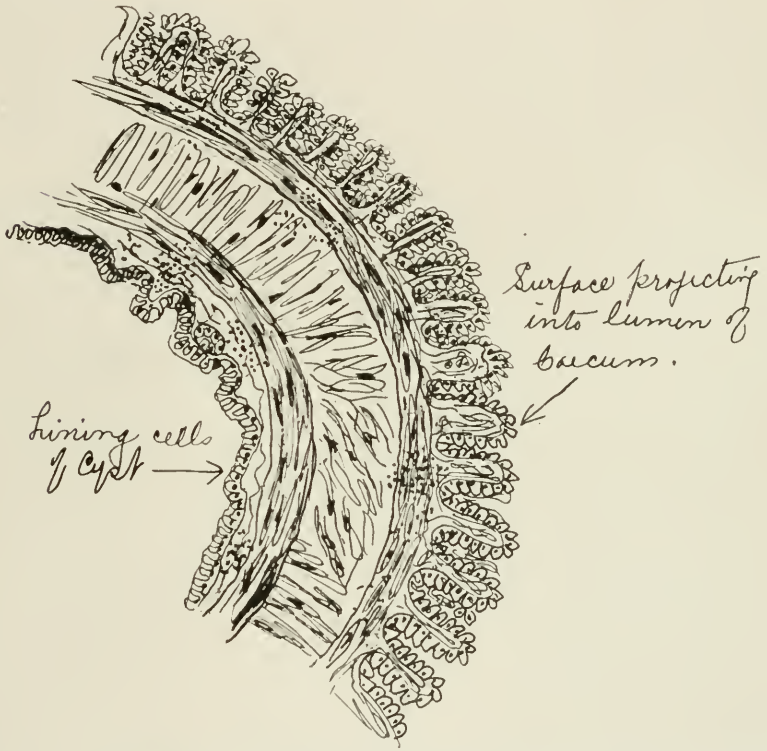

Fig. 2.—Drawing made from section through cyst, showing the internal layer of somewhat flattened epithelium, the three muscular layers, the external mucosa, and the infiltration.

The third case was one of obstruction in adult, 62 years of age, due to a cyst which appears to have been of a sarcomatous character.

The fourth case, reported by Sprengel,[5] occurred in a girl, 15 years of age, who had had occasional symptoms of temporary obstruction since

4. Kulenkampff: Centralbl. f. Chir., 1883, p. 679.
5. Sprengel: Arch. f. klin. Chir., 1900, lxi, 1032.

she was 4 years old. Operation became necessary and revealed a cyst apparently lying between the muscular layers of the intestine, and the apparent cause of an ileocecal invagination. The origin of the cyst was uncertain.

Krogius considers his case to be the fifth reported in which a congenital cyst in the intestinal wall was found to be the cause of occlusion of the bowel.

After an extensive search through literature the three cases quoted are the only ones I can find reported of retention cysts in the neighborhood of the ileocecal valve leading to obstruction and invagination.

The following cases have an associated interest, as the clinical symptoms were similar, although the pathological condition had a different origin.

Chas. A. Morton[6] reports a cyst in the interior of the cecum connected with the base of the appendix, obstructing the lumen of the appendix leading to a cystic dilation of it also. It does not appear, however, to have been a retention cyst for the mucous membrane of the cecum was said to terminate in a ridge around its base. The cyst projected into the lumen of the gut about 1½ inches and was full of amber-colored jelly. Its interior is said to have been smooth, and microscopic examination revealed no mucous membrane covering it or lining its cavity.

Neupert,[7] at the meeting of the Berlin Surgical Society, July 14, 1910, reports the case of a boy 10 years old, admitted to the hospital with a painful circumscribed swelling in the ileocecal region. On opening the abdomen a tumor about the size of a hen's egg was found in the ileum 10 cm. from the ileocecal valve. The tumor occupied the opposite side of the bowel to the mesentery, narrowing the lumen of the bowel. Its surface was smooth and its consistence tense and elastic. Numerous swollen glands were found in the corresponding mesentery. Resection of the gut was performed. The tumor was found to contain sterile pus. Sections of the wall examined microscopically showed a layer of cubical epithelium with traces of a submucosa; tubular glands were absent. Externally and internally the cyst was enclosed by the muscular layer of the intestinal wall. It was therefore regarded as a suppurating cyst, evidently of congenital origin and probably connected developmentally with the omphalo-mesenteric duct.

6. Morton, Chas. A.: Bristol Medico-Chirurg. Jour., 1887, xv. 319.
7. Neupert: Zentralbl. f. Chir., 1910. p. 714.

UNUSUAL TYPE OF ACID INTOXICATION IN INFANTS

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The term "acid intoxication" has been used somewhat loosely. In infancy and childhood it is produced under varying clinical conditions. It is generally agreed, as was shown by Langstein and Meyer,[1] that acetone in small quantities may occur in the urine of normal children. Acid intoxication results from incomplete fat and protein metabolism, due to functional or organic diseases of the liver or to carbohydrate starvation. It is generally believed that carbohydrate is an important factor in fat and protein metabolism. If the carbohydrate be absent, it is thought that oxidation is imperfect and beta-oxybutyric acid is formed. Beta-oxybutyric acid is not readily demonstrated in the urine, but this acid is further oxidized into diacetic acid and acetone. The presence of acetone is used as a clinical index for the demonstration of acidosis. Mellanby[2] and Sedgwick[3] have shown that creatin and creatinin are excreted in increased amounts during recurrent vomiting attacks. Cathcart[4] found that creatin is constantly present in the urine during starvation, and that carbohydrates given after fasting decrease the creatin, whereas fats given after the starvation increase the creatin. It is therefore shown that carbohydrates are required in normal protein metabolism, and also that the elimination of creatin and acetone is produced by similar diets. It is not proved that the production of abnormal acids of the oxybutyric series is without toxic effect. Even though we agree that they are not the primary cause of the condition, nevertheless, they may exert a secondary influence as the result of carbohydrate starvation, whether from persistent vomiting or carbohydrate-poor diet.

A. Loeb[5] recently called attention to the probable toxic effect caused by the administration of acetic acid. He showed that its use may cause acidosis or ketonuria.

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1. Langstein and Meyer: Jarb. f. Kinderh., 1905, lxi. 454.
2. Mellanby: Lancet, London, 1911, clxxxi, 8.
3. Sedgwick: Am. Jour. Dis. Child., April, 1912, 209.
4. Cathcart: Jour. Physiol., 1909, xxxix, 311.
5. Loeb, A.: Biochem. Ztschr., 1912, lxvii, 118.

It is found that acetone and diacetic acid are present under a variety of clinical conditions. In the infectious diseases acetonuria persists in spite of a considerable carbohydrate ingestion, probably due to some basic alteration in metabolism. Considerable acetone is found in the urine of children who are recovering from chloroform narcosis. Acetone also occurs in some gastro-intestinal disturbances of children not suffering from inanition. The acidosis of "recurrent vomiting" cannot be explained entirely on the basis of starvation. Acid intoxication results after certain forms of poisoning; phosphorus, which produces tissue necrosis in the liver, is capable of causing most marked acetonuria. Similarly, atropin, morphin, lead and antipyrin may cause acidosis.

In the acute infectious diseases, particularly diphtheria, scarlet fever, measles and typhoid, in prolonged starvation from any cause; also in diabetes and malignant disease, marked increase in the production of acetone occurs. Else Liefmann[6] has recently published a report on the occurrence of acetone in children suffering from spasmophilia, in which she attempts to show that the elimination of acetone is constantly increased.

The object of this paper is to call attention to a series of cases which have come under my observation during the past several years. They were severe types of acid intoxication, and usually terminated fatally. They occurred mostly in previously healthy children at about the weaning period. In most instances the infants came from healthy parents. In one family two children had died from this affection. The third child, whose history will be given below, was similarly attacked, but recovered after a severe illness. Dr. Wesley F. Orr of Idaho[7] reports five children in the same family who died with symptoms similar to those which I am about to describe. These cases lead us to believe that there is a familial type of the disorder.

CHARACTERISTICS OF THE DISEASE

The illness usually occurs in large, robust, previously healthy infants. In some cases the children show a stationary weight-curve for several weeks before the onset. If fed at the breast, they show signs of hunger and dissatisfaction with the food because the breast milk is scanty or of poor quality. Some of the infants in this series were artificially fed for weeks or months before the onset of the illness.

6. Liefmann, Else: Jarb. f. Kinderh., lxxvii, part 2.
7. Orr, Wesley F.: Personal communication.

The disease is ushered in by gastro-intestinal symptoms, consisting of more or less diarrhea and nearly always vomiting. The patients are at first restless and show moderate febrile reaction during the first days of the illness, rarely exceeding 101 F. Later on the temperature tends to be lower, averaging between 99 and 100 F. On the second or third day there is some abdominal distention, dyspnea, with rapid respiration and an increase in pulse-rate. The respirations are labored, and the accessory muscles of respiration show marked activity. The liver is markedly enlarged, the edges are plump and the surface firm. The urine soon contains albumin, and hyalin and granular casts, without blood, with acetone and diacetic acid. In one of my cases leucin and tyrosin were also found. The urine contains no sugar.

About the third day stupor is noted, which gradually deepens into coma. The blood shows no pathological changes, the leukocytes vary between 9,000 and 12,000, and the differential count shows no variation from normal. Toward the close of the disease intestinal atony may occur. As a result, no feces or gas are passed voluntarily, nor can any intestinal evacuation be induced by mechanical or therapeutic agents. Abdominal distention increases progressively, and cyanosis and dyspea are marked. Unconsciousness continues and occasional vomiting persists until the end. The reflexes are present and normal. There are no symptoms of cranial nerve involvement and usually no pulmonary complication. When death takes place it usually occurs in four or five days after the onset.

I shall report several typical cases from my clinical records. I have notes on nine cases, not including the severer types of cyclic vomiting, with presence of large quantities of acetone and diacetic acid. In passing, I may say that a typical case of cyclic vomiting occurring in my practice proved fatal, though such cases are not included in this report.

CASE REPORTS

CASE 1.—The first case of this unusual type of acid intoxication came under my observation Sept. 1, 1902. The patient was one year old; the father was a physician. On August 30, after the infant had been nursed, she was taken seriously ill with vomiting. She vomited several times during the night: first food, and later on a clear watery fluid. The father administered one grain of calomel in divided doses and other mild laxatives. The child's bowels moved the next day, and she passed gas, though the vomiting continued. On September 2 the following notes were made: Well-nourished female child; slight evidence of rickets; some roughness of the respiratory note over the right upper lobe. respirations rapid; pulse full, strong, moderately accelerated. Temperature,

99.5 F. Examination of the head, mouth, pharynx, and glandular system of the neck proved negative. The liver was enlarged and felt doughy; abdomen flat; spleen not palpable; no evidence of tumor in the abdominal cavity. There were no meningeal symptoms, though the child was inclined to be stuporous. The following day it was noted that the child was obstinately constipated; the vomiting continued and the abdomen had become slightly tympanitic. The expiratory note in the right upper lobe was an exaggerated vesicular type, though there was no dulness on percussion. On observation it was evident the child suffered from abdominal pain. She was inclined to sleep, though she could be aroused. It is worthy of note that while the temperature was low the pulse was of good quality, though accelerated, and the respirations were extremely rapid, somewhat noisy and superficial. Later in the evening it was thought that the child passed gas, though there had been no fecal evacuation during the day. She had been given a simple non-irritating diet. Water was vomited shortly after being given. On the morning of the fifth day the patient developed alarming symptoms, and the father sought the advice of a neighboring physician. The child had not evacuated its bowels for twenty-four hours, and because no gas had been passed, the physician who was summoned concluded that the primary difficulty was a mechanical obstruction of the intestines, and surgical consultation was called. At this consultation the opinion was expressed that the child was suffering from intussusception. This later proved to be incorrect. The following morning the infant's respirations were rapid, pulse feeble, abdomen tympanitic, and the child was plainly in collapse. The urinary examination showed acetone and diacetic acid, a trace of albumin with casts, and an evaporated specimen showed leucin and tyrosin. During the day the child grew progressively worse; stimulation was employed without effect. A careful abdominal and rectal examination gave no evidence of intussusception, nor any other form of mechanical obstruction of the bowel. Crepitant râles were heard over the right upper thorax.

September 4 the child died at 7 p. m.

September 5 autopsy was performed with the following findings: The abdomen contained no free fluid; the peritoneum was smooth, shining and somewhat injected. The great omentum and the mesenteric glands were normal. A systematic examination of the bowel showed no adhesions or inflammatory reaction in the mesentery or in the serosa covering the bowel; no intestinal obstruction of any kind or nature; mesenteric glands were not enlarged. The spleen was about normal in size, and presented no pathological change. The liver was striking, because it was markedly increased in size, and presented a light yellowish terra-cotta appearance.

The liver on section showed that the surface was glistening, decidedly yellow, and the knife was greasy because of the fatty nature of the tissue.

The capsule of the kidney stripped readily. The cortical markings were obliterated; turbid urine exuded from the pelvis. There was no vascular engorgement, though fatty changes were present.

In the intestine an occasional Peyer's patch stood out prominently, and was the site of an inflammatory reaction.

The lungs showed small areas of focal inflammation and congested at the bases.

The heart muscle was light in color, though it was well contracted. The valves were normal.

The histological study was made by the late Dr. Howard T. Ricketts. His report is briefly abstracted herewith: A study of the liver showed that the

markings of the lobules were not distinct. There was no increase in the connective tissue of the liver. The liver cells stained poorly. Fatty degeneration of the parenchymatous cells was extreme and widespread, being more marked in the periphery of the lobules than in their centers. Little protoplasm was left in such cells, and what remained was granular. The center of the lobules showed marked granular degeneration. There were also many small areas where neither the nucleus nor the cell body was stained; no normal liver tissue was seen. Many large bacilli not staining by Gram were present, but had no distinctive distribution. In the lungs the vessels were congested. There were certain areas in which the air cells were filled with red-blood corpuscles, though there were a few leukocytes among the extravasated red cells. Moderate fatty degeneration was found here and there in the parenchyma of the kidneys. There were no hemorrhages.

Summarizing the histological findings one notes:

Heart: Moderate focal necrosis.

Lung: Acute hemorrhagic lobular pneumonia (Diplococcus pneumoniae, probably). Moderate necrosis of epithelial cells. General pulmonary congestion.

Liver: Extensive granular and fatty degeneration, the picture resembling acute phosphorus poisoning.

Kidney: Acute granular and fatty degeneration of the parenchymatous tissue.

In my series of nine cases four autopsies were performed, with findings like those described above, the predominating feature being fatty degeneration of the liver and other organs.

CASE 2.—A male child, aged 1 year, who had been previously weaned and was receiving artificial food, entered the hospital Aug. 1, 1911. He was taken sick three days previously, suffering from moderate diarrhea, having three to five stools daily. The baby vomited several times after nursing. A slight fever was observed during the first day of the disease. He had been restless, cried much of the time and suffered from abdominal distention. On the third day of the illness he developed a mild stupor. The mother becoming alarmed, sought the hospital. On admission it was noted that the baby was well-developed, well-nourished, and was breathing rapidly and superficially; pulse, 172; respirations, 49; temperature, 101.4 F. Examination of the heart and lungs was negative. The liver was distinctly enlarged; the spleen was not palpable; the abdomen was moderately distended. In a short time the temperature was found to be 99 F., pulse 160, and respirations 40. The urine was acid, contained a faint trace of albumin, no sugar, though a marked quantity of acetone and diacetic acid, an occasional leukocyte, but no red cells. The baby died twelve hours after admission to the hospital. No autopsy was permitted.

CASE 3.—Oct. 2, 1911, a physician brought his child to us from a neighboring city. A male child, 11 months old, had made phenomenal gain in weight. At 7 months of age he weighed twenty pounds. After the seventh month he remained stationary in weight. For the past three weeks the patient had been unable to satisfy his hunger at the breast. He was nursed every hour to every hour and a half, whereas, previously he had been nursed every three hours. The mother noted that her breast milk had been scarce, and that she herself had lost in weight during the past several weeks. Four days before admission to the hospital he was weaned from the breast. He refused all nourishment and took only water. For the next few days he took little or no food. The bowel

movements were regular and he urinated frequently. On October 1 he became constipated, and had no bowel movement; previously he had two or three evacuations a day. On October 2 he started to show signs of dyspnea, the respirations became rapid, and later in the day he became stuporous, with a pulse of 140. Constipation persisted, and he continued to refuse all kinds of food except water, which he desired at frequent intervals. He vomited every three or four hours. The examination was for the most part negative; the abdomen was slightly distended; the liver extended three fingers' breadth below the costal arch, and seemed doughy on palpation. The urine contained albumin, hyalin and granular casts, and acetone and diacetic acid in abundance. He succeeded in having several bowel movements on the day of admission, and expelled some flatus. The treatment consisted of the administration of sodium bicarbonate solution by mouth; atropin, grain 1/1000 by mouth; twenty drops of brandy, repeated at short intervals; and strained oatmeal-gruel was used as food. In addition to the above a solution of sodium bicarbonate was given subcutaneously, and 8 per cent. of glucose in normal salt solution was given by rectum, using the drop method. He died Oct. 3 at 1:45 p. m. No autopsy was permitted.

CASE 4.—H. B. T., male child, aged 6 months; was born normally; weighed 8 pounds; gained steadily in weight; erupted first teeth at 4 months; had six teeth at 6 months and sat erect. Was a large, strong, robust child; had mother's milk exclusively since birth. Was somewhat colicky during the first month of life, and since four weeks of age had been nursed five times in twenty-four hours. No other foods were given; no fruit or vegetable juices. He never had a sick day until the onset of the present illness. Three days before admission to the hospital he weighed 20 pounds 4 ounces, having gained 5 ounces in the past week. The bowels moved once or twice a day, and the movements were normal. The baby always slept well and showed no urinary symptoms. On the first day of the illness the stool contained mucus, and was of a greenish color, though the infant appeared as well as usual. The next day the infant again had two bright green stools, though he appeared well. The third day the infant had another greenish stool, but since that time (twenty-four hours) had had no bowel movement. Cried at intervals and seemed restless and uncomfortable. At 6 a. m. Sept. 26, 1912, it was noted that the child began to breathe rapidly and heavily, became languid and drowsy, passed very little urine and bowels became obstinately constipated. He became cyanosed, had a drawn expression of the face; slight fever, 99 F.; pulse, 120.

Family History.—The father suffered from headache since boyhood; the father's mother had had headaches; the father's father died from alcoholism; a brother was epileptic. The mother stated that her health was perfect in every way; no chronic disease and no tuberculosis. The mother's sister has a goiter. Her parents are living and well. The patient has a sister 5 years old, who always has enjoyed good health. Two children in this family died from a condition resembling the present attack of the patient. The first child lived eleven months, was being weaned, and was having a few bottles of cows' milk daily in addition to breast feeding. The baby had been on mixed feedings for three weeks, when he showed signs of indigestion, with greenish stools, though he was not severely ill. After persisting three or four days the patient suddenly was seized with rapid breathing, followed by stupor, and he died in forty-eight hours. The second child, a boy, aged 9 months, very large and well-developed, died eighteen months previously; was fed at the breast, and was given one bottle a day. This feeding had gone on for three or four weeks. At the expiration of this time he

showed signs of indigestion, with greenish, mucous stools, and within a few days began to breathe rapidly, was stuporous, bowels were constipated, and on the fourth day he went into coma, and remained comatose until death, which occurred on the sixth day.

The third baby of this family, the subject of this clinical record, was admitted to the hospital Sept. 26, 1912; temperature, 101 F.; pulse, 120; respirations, 36. The respirations were rapid and superficial; the infant was cyanosed. The general examination of the head and thorax was negative. The liver was enlarged, though the spleen was not palpable. The reflexes were all somewhat exaggerated. The skin showed a peculiar, pasty appearance. There was no edema. The stools were slightly increased in frequency, greenish and watery, and of a peculiar, penetrating, sour odor. The child was irritable and restless at times, and often fell into a profound sleep. In order that I might study the condition accurately, the mother's urine was collected, and her breast milk was subjected to various examinations. Examinations of the *mother's* urine made on the first day of admission to the hospital showed: specific gravity, 1.030; faint trace of albumin; 0.7 per cent. sugar; trace of acetone; no diacetic acid; a few epithelial cells; few leukocytes; no casts; the fermentation test for sugar was negative. The *infant's* urine, examined about the same time, showed a faint trace of albumin; no sugar; acetone and diacetic acid; ammonia, 0.0952 per cent. On testing the baby's urine with the polariscope and by chemical methods no sugar was present. The sugar rapidly disappeared from the mother's urine. A tolerance test for sugar in the mother was made by the ingestion of 140 grams of sugar; urine taken two and four hours afterward showed no sugar by Fehling's test or the polariscope.

For the next few days the infant was extremely ill: showed abdominal distention, vomited occasionally and had a tendency to be drowsy. On October 1 he became much worse: respirations were increased; pulse small and intermittent; on account of what seemed *a disastrous* collapse, he was given a 2 per cent. solution of sodium bicarbonate subcutaneously in the interscapular region. An examination of the urine at this time showed that it was alkaline, with marked acetone and diacetic acid reactions. After a precarious night the baby seemed better next morning, though the area where the subcutaneous injection had been given showed a marked tendency to gangrene and sloughing. The following day the baby presented general edema; puffiness of the face and scrotum; the skin everywhere edematous; no albumin in the urine; and the acetone and diacetic acid were markedly less.

The mother's milk showed 5.5 per cent. of fat; no acetone or diacetic acid. The milk was fed to a kitten, and was injected subcutaneously into guinea-pigs and rabbits without in any case producing the slightest toxic effect. No acetone or diacetic acid was recovered from any of the animals that were tested. After ten days of severe illness the edema disappeared, the patient gradually became playful and happy, and except for the large slough between the scapulae, was perfectly comfortable.

The treatment consisted of *weaning the baby from the breast milk*, giving rectal infusions of eight per cent. glucose in normal salt solution, large doses of sodium bicarbonate by mouth, of whisky, or sour wine in half-dram doses every two hours, soy-bean soup three times a day; occasional oxygen inhalations when cyanosis and dyspnea were most marked; and the subcutaneous infusion of sodium bicarbonate. Levulose and sodium bicarbonate were given by mouth. The patient made a complete recovery, and has progressed up to the present

time, with an occasional upset. The mother makes almost daily examination of the urine, testing for acetone and diacetic acid, and on one or two occasions has discovered the faintest trace. Aside from this the patient has remained well up to the present time.

The interesting points about this case may be summarized as follows: Previously healthy baby was taken suddenly ill with gastro-intestinal symptoms, diarrhea and vomiting. Enlargement of the liver, followed in a few days by rapid breathing and a marked quantity of acetone and diacetic acid in the urine. The baby showed irritability and discomfort, and at times a tendency to coma, and finally made a complete recovery.

The most striking feature of this case was the fact that two other infants of this family had previously fallen ill the same way and had died. It is noteworthy, too, that the mother showed some urinary changes on the admission of the infant into the hospital. Though normally a calm and self-possessed woman, she was suffering from the most intense suppressed emotion because she felt that she was about to lose her third child in the same way that she had previously lost two. Possibly this may explain the glycosuria in her case. At any rate, it soon disappeared, and her breast milk, which was examined chemically and injected and fed to animals, as already stated, gave no toxic reaction.

It may be thought that these cases bear a clinical identity with cases of cyclic vomiting; but in this type vomiting is not so persistent, and sometimes scarcely occurs at all. In my series of cases of "unusual acid intoxication" the disease described occurs in young infants, often toward the close of lactation.

Persistent and uncontrollable emesis characterizes the cases of cyclic vomiting. Rapid, superficial breathing, enlargement of the liver, low temperature and rapid pulse, with the occurrence of tympany, obstinate constipation, with little or no vomiting toward the end, are features of the type which I am now describing.

A series of cases similar to those which I have enumerated were described by Dr. Thomas D. Parke[8] of Birmingham, Ala., before the Section on Diseases of Children at the meeting of the American Medical Association in 1907. Dr. J. Ross Snyder of the same city has seen the same class of cases and has made verbal reports to me. They were mostly in infants who varied from 6 months to 20 months of age. Most of Parke's cases were breast-fed, though a few were artificially nourished.

8. Parke, Thomas D.: Jour. Am. Med. Assn., 1907, xlix, 1827.

In the literature one finds scant mention of this extreme form of acid intoxication in infancy. Possibly some of the severer forms have been described as cases of acute yellow atrophy of the liver, though in none of our cases was jaundice present. The liver remained constantly large, not atrophied, as in cases of acute yellow atrophy. The presence of leucin and tyrosin is not pathognomonic for acute yellow atrophy, since both substances may be found in small amounts in urine in extreme degenerative diseases of the liver, such as afebrile jaundice with slight hepatic enlargement, leukemia, typhoid fever and other diseases.

From the urinary findings, from the symptom-complex and from the almost universally fatal termination we are justified in assuming that some profound intoxication has taken place in the infant's organism. The symptoms which this disease group represents have suggested resemblance to the so-called "milk sickness," a condition which has been observed throughout the pioneer portions of the United States where cows became ill with the so-called "trembles," and human beings who partook of milk from such animals or ate their flesh fell ill with a diseased condition which resembled, in some respects, the cases which we are describing. Human beings ill with this disease show languor, loss of appetite and extreme constipation, usually marked nausea; the breath has a peculiar, sweetish odor. The pulse is quick, full and soft, and the patients have little or no temperature; drowsiness and coma are not uncommon, and irritability, convulsions and marked delirium may occur. Notwithstanding the resemblance, those cases which we report, as well as those reported by Parke, were for the most part breast-fed infants by healthy mothers.

These cases occurring frequently toward the close of the period of lactation lead us to ask whether there was some quantitative change in the breast milk sufficiently marked to produce the condition of starvation. Thus in the third case mentioned the baby had not gained weight for four months before he came under observation, and for three weeks previous to admission into the hospital he had appeared unable to satisfy his hunger while at the breast. For this reason he had been nursed every hour or hour and a half, whereas previously he had been nursed every three hours. Could a starvation acidosis have resulted, or was there some deficiency in the component parts of the breast milk which could have led to a severe intoxication?

Referring to Case 4 (H. B. T.), the baby was plump and rotund, was receiving large quantities of breast milk, and indeed all of the infants who came under observation were well developed, usually above the average. One would hardly conceive that these infants were in a condition of starvation, especially if they be compared with the cases of marasmus and decomposition which one so frequently sees as the result of prolonged food deprivation without any evidence of the extreme acid intoxication, or the fatty degeneration of the internal organs which we found in our series of cases. Or is the condition possibly due to a toxicity of the food per se? All of the animal experiments which we made showed the milk to be free from poisonous effect. It may be held that this proof is insufficient and that the small animals may have remained free from toxic symptoms, whereas the baby might have succumbed. The milk was injected in considerable quantity in guinea-pigs and rabbits and was fed to kittens. We would have expected some results if toxic products had been present. In addition, some infants, as has been pointed out, were exclusively breast-fed, while others were being artificially nourished. We conclude, therefore, that the cause did not reside in the toxicity of the food before ingestion.

Dr. Parke in his paper suggests the possibility of a bacterial origin because of the usual absence of high fever and moderate leukocytosis. As one studies these cases he becomes impressed with the fact that the disease seems less likely to be infective or bacterial in origin than a profound metabolic disturbance. Leucin and tyrosin were found in one of our cases marked by extreme fatty degeneration of the liver. The production of these substances may be explained by the destructive cellular changes in the liver, or may be due to a breaking down of the proteids into amino-acids, and of these acids into leucin and tyrosin. In the severer cases of acute yellow atrophy these amino-acids are present in the liver as well as in the blood and in the urine, and hence leucin and tyrosin may be formed outside of the liver in other organs.

The case which recovered under treatment received considerable proteins in the form of casein, gelatin, soy-bean flour and the animal broths, together with carbohydrates. We assumed that the patient had an intolerance for fat, consequently carbohydrates were given in abundance in the form of cooked starch and levulose. It is possible that the protein of the food was the toxic agent, though in our plan of feeding during the convalescence the protein disturbances seemed to act not

unfavorably. Nor do we think that the condition should be considered in the light of an anaphylaxis, for many of the infants received the proteid in the form of breast milk. It may be suggested that the carbohydrate intake was insufficient to protect the fat and proteid metabolism, and possibly in this way a perversion of metabolic process occurred, so as to give rise to incomplete or toxic products, with a consequent acidosis and subsequent tissue degeneration.

Recent work has shown that toxic substances can be obtained from every protein that has been subjected to hydrolysis. This includes egg-white casein, as well as bacterial proteins. Jobling and Bull[9] have demonstrated that in bacterial proteids, probably in all protein substances, the toxic products are found in the proteose fraction of the split products (one of the first products of protein cleavage). It has also been shown that under certain conditions the epithelial barrier of the intestines permits the large protein molecule to pass through. This has been demonstrated by the use of egg-albumin, giving rise to an alimentary albuminuria when small doses of protein were administered by mouth.

In seeking to assign a suitable cause for these unusual types of acid intoxication, it has seemed to me—from clinical experience, some experimental work and therapeutic results—that the disease in question depends on some derangement of the infantile metabolism, resulting in the production of toxic products from misdirected chemical processes.

The analogy based on the familial occurrence of the disorder in one of our cases leads us to note that an inherent weakness of cells or organs may exist, as in diabetes mellitus, where a marked predisposition to the disease occurs among entire families.

The cases reported by Parke, already referred to, seem identical with those contained in this report.

If I have described a disease group which has been previously classified or reported under another name, the literature has been inaccessible to me, or has not come to my notice. At any rate, the current textbooks and periodic literature make no mention of these cases.

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9. Snyder, J. Ross: Personal communication.

ACUTE LYMPHATIC LEUKEMIA

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NEW YORK

Acute leukemia is not as infrequent as might be inferred from the relative scarcity of reported cases in medical literature. In view of the similarity of the prominent symptoms of this condition to those present in several other not allied affections, the disease, in the absence of blood examinations, has been frequently overlooked.

The predominating evidence of hemorrhages from various mucous membranes has apparently justified the diagnosis of morbus maculosis Werlhoffii or scorbutus. Thus Laache of Christiania points out that some cases which a few years ago have been called scurvy, are really acute leukemia with excessive pseudoscorbutus stomatitis. Some of the reports labeled sporadic scurvy, in his opinion, ending fatally after a comparatively short course, are in reality undiagnosed acute leukemia.

Considerable interest centers in the condition of the gums. Henry Jackson[1] reports two cases attributed, when the illness was first observed, to some local disturbance of the gums and mouth. In each case a rapid loss of strength followed the local trouble about a tooth. Case 2 was admitted to his ward as one of possible scurvy.

It has also been confounded with hemorrhagic septicopyemia, with anemia or malignant diphtheria, in cases where ulcerative processes of the tonsils and pseudomembranes existed.

"Of special interest is the resemblance that some cases bear, particularly those without enlargement of the lymph-nodes, to typhoid fever." Microscopic examinations of the blood and other organs are essential aids in determining the differential diagnosis. An examination of the blood should be made in every case of purpura. If this is done, the existence of leukemia can be definitely determined.

August Strauch,[2] in his careful study of a case, has reviewed the literature up to the present. I am indebted to this most excellent article for many valuable points of interest in this paper, practically a résumé of his work.

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1. Trans. Assn. North American Physicians, 1911.
2. Strauch, August: Am. Jour. Dis. Child., January, 1913.

The disease has been observed in a female infant with fatal termination nineteen days after birth, and, on the other hand, in a man 73 years old. The symptomatology varies with the more or less rapid progress of the disease. The course may be rapid, ranging from a few days to several weeks, or exceptionally a few months.

The onset is frequently abrupt, less often insidious, preceded by lassitude, weakness, pain in neck or head, increasing pallor, shortness of breath, fever, etc.

In other cases, pains in the extremities or joints (simulating acute rheumatism), painful sensation in the splenic region and perhaps violent epistaxis or hematemesis, point to a blood dyscrasia. Not infrequently hemorrhagic necrotic ulcerative changes of the buccal mucous membrane, gums and tonsils or edema of the face are the first symptoms.

The appearance of hyperplasia of the lymphatic organs, the spleen, lymph-nodes, the lymphoid structures of the oropharynx and other lymph adenoid tissues should arouse suspicion as to the nature of the trouble.

The most striking clinical manifestation, however, is the hemorrhagic diathesis, expressing itself by hemorrhages into the general integument, the subcutaneous tissues and bleeding from the mucous membrane of the mouth and nose and the urogenital and gastro-intestinal tracts. Hemorrhages into the brain, muscles, nerves, eye, ear, etc., have been reported.

Three principal types have been described by Gilbert and Weil, though the diverse pictures may overlap.

1. The rare "typical" acute leukemia, with enlargement of the lymphatic apparatus as the predominant feature.

2. The hemorrhagic form, characterized by an intense hemorrhagic diathesis.

3. The buccapharyngeal, i. e., the anginous and pseudoscorbutic form with hemorrhagic infiltration and necrotic ulcerative processes in the oropharyngeal cavity. The diagnostic symptom in these cases is the increase of the white blood-corpuscles in the circulation, particularly the lymphocytes. In the beginning, the changes may be only slight. The variation in the number of leukocytes may be considerable, ranging from several hundreds of thousands, or less than 100,000 to below 10,000 with even leukopenia. The principal and diagnostic characteristic of the blood in a case is the relative increase in the number of lymphocytes.

The polymorphonuclear neutrophils constitute but a small percentage. In one of our cases but two were found in a count of 500 white blood-cells.

As a rule, the macrocytic forms of lymphocytes are in excess. Under the influence of intercurrent diseases (pneumonia, sepsis, diphtheria, suppurative otitis) the blood may even become leukemic.

Case of acute microlymphatic leukemia have been recorded in a number of instances. The existence of an acute myeloid leukemia in children has been established by a series of well-observed cases. Panton and Tidy[3] have directed attention to the existence of acute myeloid leukemia. They bring evidence to show that there is no sharp line of demarcation between the lymphatic and the splenomedullary type. Sometimes a patient, who has heretofore presented the characteristics of the latter, may toward the end offer a changed blood-picture, and, if seen for the first time, might easily be regarded as a sufferer from the lymphatic form. Atypical cases are differentiated with difficulty, for in very young children a relative lymphocytosis exists.

In addition to the symptoms referred to above, the liver is enlarged, spleen likewise, and progressive emaciation and cachexia are noticeable.

The discussion of the therapy is brief. Atoxyl and salvarsan (tried also in Dr. Saxl's case) are of no avail. Roentgen ray also has failed.

To quote Strauch: "Unfortunately, the words of Gilbert and Weil hold true, that the physician has done his utmost in making the diagnosis, since this involves, as it seems, *quod vitam* an absolutely bad prognosis." A rare curable form has been described by Turch. He is led to believe from a study of four cases which recovered that a close genetic relation may exist between an acute infection originating in the tonsils and a "lympholeukemia reaction on acute infection."

In this connection it may be of interest to refer to a recent article by R. C. Cabot,[4] who, discussing the lymphocytosis of infection, gives the following summary:

"1. Wound sepsis, boils and wide-spread streptococcic adenitis of tonsillar origin may be accompanied by a lymphocytosis so pronounced as to suggest lymphoid leukemia.

"2. No reason is known for this substitution of lymphocytosis for the usual polynuclear leukocytosis of infections.

"3. The distinction between such a lymphocytosis (accompanying a wide-spread adenitis) and leukemia depends on the recognition of an infectious origin for the adenitis, on the lesser degree of lymphocytosis in the infectious type and on the course of the disease."

3. Panton and Tidy: Lancet, London, 1912, No. 1, p. 1328.
4. Cabot, R. C.: Jour. Am. Med. Assn., March, 1913.

But little is known in regard to the etiology of acute leukemia. It has been classed among the sarcomas. The majority of authorities refer the cause, particularly of the acute form, to infection.

In the three cases reported below, a badly ulcerated tooth and tonsillar abscess preceded the trouble in one case; in the second a badly crushed finger existed, and in the third multiple abscesses had occurred. Acute infection starting from the tonsils or adenoids is believed to have been the cause in a few patients who have recovered with lympholeukemic reaction of acute infection.

Pyogenic agents, as streptococci and staphylococci, appear to prevail in most of the cases. Spirochetes were found in the fluid obtained by aspiration from the lymph-nodes. Animals inoculated by cultures from the blood of two patients who have died of acute myeloid leukemia have shown characteristic blood changes.

Positive results have been attained by inoculating a healthy dog with an emulsion of fresh bone-marrow and spleen from a dog afflicted with acute myeloid leukemia.

Staphylococcus albus cultivated from leukemia in man has produced leukemia-like blood pictures in four cases after inoculating dogs and monkeys. Other interesting animal experiments are referred to by Stranch.

CASE 1.—For the following history, and opportunity to see the patient, I am indebted to Dr. Josef Saxl. Male, aged 14 years, born in New York of Russian Polish parents, lived under favorable sanitary and social conditions. He had the usual ailments of childhood. The past summer while at the seashore he developed a large number of abscesses over various parts of the body; these were operated on and healed without trouble. In the latter part of September the boy was reported to be in fair condition, apparently well nourished, though somewhat jaundiced (?) and anemic. The yellowness disappeared in a week. When seen again October 31 at his own home in the city, he presented a high grade of anemia, was short of breath, had some nose bleeds, appetite lost, constipation present. The cervical and inguinal glands were enlarged, though not tender. Heart action rapid and irregular, pronounced myocardial weakness with loud murmurs over the precordial region. Spleen greatly enlarged, extending to the median line. Liver likewise considerably enlarged.

Blood examination.

Red blood cells	2,000,000
White blood cells	800,000
Hemoglobin	40 per cent.

Dizzy spells, general weakness and tottering gait noted.

Under treatment there was some slight improvement. November 6 another severe hemorrhage occurred from the nose with vomiting of blood and sudden

collapse. Pulse rate reached 200, thready in character. Rallied somewhat. November 9 there was a repetition of the above symptoms, the vomiting was distressing and persistent, necessitating rectal feeding.

Excessive weakness persisted. On the 16th another severe nose bleed occurred, from which he rallied somewhat, but the same night an internal hemorrhage with vomiting of blood caused a fatal outcome. Temperature was irregular in type, running between 98 and 103 F.

Blood examination November 9:

Red blood cells	1,500,000
White blood-cells	750,000
Few nucleated red cells.	
Hemoglobin	30 per cent.
November 14 only	25 per cent.

Five hundred white cells counted revealed:

Small mononuclear	425
Large mononuclear	73
Polynuclear	2

No autopsy.

CASE 2.—Harry S., 4¾ years of age, born in New York. Admitted to the children's service Beth Israel Hospital June 25, 1912. The family history was unimportant. With the exception of measles, preceded by chicken-pox in April, 1912, the patient had enjoyed fair health. About three weeks ago the right ring finger was caught in closing a door and bruised.

The present illness, as far as can be determined, was supposed to have begun a week later, when a paronychia formed about the contused finger. The distal and middle phalanx turned dark blue in color, became tender to the touch and increased in size, but remained quite soft. The nature of the dressing could not be ascertained. About this time chilly and feverish sensations were reported, accompanied at times by profuse sweating. Father noted that child coughed and expectorated thick greenish mucus. Seven days before admission marked swellings of the glands about the size of a fist, which have since decreased in size, appeared on either side of the neck.

In addition, patient became pale and dyspnea set in. Three days before admission the family physician called the attention of the parents to enlarged glands in both axillae and inguinal regions. Ecchymotic spots were seen by the father on the right side of the back and right lower extremity, but he had not noticed any purpuric spots over the dorsal aspect of left upper extremity until his attention was called to them at the time the patient was examined at the hospital.

Patient was fairly developed, no edema or cyanosis present. Pallor of face and surface generally was pronounced, with a peculiar wax-like tint due to the marked anemia. In addition the skin felt cold and dry, numerous purpuric spots varying in size from one-sixteenth to one-eighth inch were found. A few large ecchymoses were detected over the buttocks.

Pupils equal and react. Both eyes prominent, left more so; in addition there is some subconjunctival hemorrhage on this side. The exophthalmus was marked and was explained by hemorrhages deep in the orbit.

Ears, nose and mastoid negative. Teeth in fair condition. Moderate hyperplasia of gums, some bleeding, mucous membrane pale. The axillary and inguinal nodes were moderately enlarged. Submaxillary gland was about the

size of a walnut; post-cervical also involved; epitrochlear palpable. Heart and lungs negative.

Abdomen enlarged and distended. Liver dulness extends from about fourth interspace to line with the umbilicus. Spleen enlarged and hard, palpable as far down as level of umbilicus.

The injured finger was in a condition of dry gangrene (distal and middle phalanges involved). June 28: Blood culture. Wassermann; nose and throat cultures negative.

	June 25	June 26 Poikilocytosis	July 2 Poikilocytosis
Red blood cells	1,400,000	1,400,000	1,160,000
White blood cells	30,000	31,200	8,600
Small mononuclear	37%	33%	5%
Large mononuclear	55%	60%	88%
Transitional	....	3%	1%
Polynuclear	6%	2%	4%
Eosinophils	2%	2%	2%
Hemoglobin	55%	55%	....

Coagulation time less than eight minutes.

July 2: The exopthalmus of the right eye has increased. Stool shows positive guaiac (no meat given). July 4: Severe hemorrhage from the oropharynx and alimentary canal, followed by collapse and fatal ending about the twenty-third day of the disease (as well as could be determined).

The temperature ranged between 101 and 98.8 F., irregular in type. Pulse, 110 to 140.

CASE 3.—Morris F., school boy, aged 9 years, native of Austria. Admitted to Gouverneur Hospital October 20, 1911, and transferred to Medical Service October 30.

Family history unimportant. For years the boy has had trouble with his tonsils and has been a mouth breather. In June, after considerable suffering, a peritonsillar abscess was incised. There is also a history of "some swellings of both sides of the neck." A week later he developed diphtheria. Was taken to the Riverside Hospital, and four weeks ago was sent home. Since then he has constantly complained of pains about his heart and had frequent attacks of "apparent suffocation." In addition to this he had the same nasal trouble, but did not complain of his throat. He grew progressively worse, the attacks became more frequent and finally he was brought to Gouverneur Hospital. During the past week the boy has had a chill every forenoon, then felt feverish in the evening. The mother further states that for the past three weeks he has been constantly coughing and sweated a good deal at night. There has been considerable loss of weight since.

On admission, the patient was fairly well nourished, rather pale, with a herpetic eruption about the nose and lips. The buccal mucous membrane was markedly anemic with grayish-white flaky deposits on the mucosa. The gums showed considerable hyperplasia, presented a spongy and unhealthy appearance, bleeding easily when touched.

At the junction of the mucous surface of the lower lip on the right side and involving the alveolor mucosa, a greenish foul-smelling slough was noted, the right lower molar was extensively decayed, the adjoining gums were swollen, red and exquisitely tender. The submaxillary glands were enlarged, but did not show any fluctuation or tenderness.

Ears appear normal; at times there is a slight watery discharge from the nares. The tonsils are enlarged. Intense pain present in the throat and patient cannot chew or close his mouth because of the condition of his gums and molar tooth.

The posterior cervical, post auricular, axillary and inguinal glands were quite large. The glands in the submental triangle and at the angle of the jaw, particularly on the right side, were extensively involved, without any evidence of inflammatory reaction or matting together. The integument presented the waxy pallor characteristic of pronounced anemia, with an icteroid tint of hemolytic nature.

The apex beat was not visible: there was an indistinct diffuse fluttering impulse slightly below and within the left nipple. The heart sounds are slightly irregular, faint and indistinct; over the precordial area a soft blowing systolic murmur is transmitted to the left (probably of myocardial origin).

Pulse slightly irregular, compressible and at times almost inperceptible.

Chest: On the left side, at the base posteriorly the physical signs are those of slowly resolving pneumonia. Spleen palpable, liver slightly enlarged. Temperature irrregular, varying from 100 to 104 F. Nose and throat culture negative. Urine negative.

Blood: Red blood cells	1,370,000	
White blood cells	47,000	
Hemoglobin	35	per cent.
Lymphoid marrow cells	42	per cent.
Large lymphocytes	25	per cent.
Small lymphocytes	20	per cent.
Polynuclear	3	per cent.
Large mononuclear	6	per cent.
Myelocytes	4	per cent.

Since admission the boy has had several chills and complains of severe pains over the right side of face and jaw. Periods of depression, with difficulty of breathing and pericardial pains, restlessness and moaning are reported. At times there seemed to be a slight improvement in his condition. Though less complaints are made and the swelling of face has diminished, there is increasing weakness with more pallor.

October 31, death occurred suddenly from hemorrhage, the blood pouring from his mouth. As an autopsy was refused, the seat of hemorrhage could not be determined.

As the principal characteristics of the disease have been brought out in the histories, but few comments are necessary. Attention may be directed to the very large proportion of white cells present in Dr. Saxl's case—800,000 white blood-cells to 2,000,000 red blood-cells; 750,000 white blood-cells to 1,500,000 red blood-cells—with only two polynuclears in a count of 500 white blood-cells.

Case 2 accentuates a point brought out by Osler and others—the importance of repeated blood examinations. In this case, while under observation, the cells varied from 31,200 to only 8,600. This is often seen in terminal infections.

PURPURA, URTICARIA AND ANGIONEUROTIC EDEMA OF THE HANDS AND FEET IN A NURSING BABY

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I wish to report a rare type of purpura and urticaria associated with angioneurotic edema of the hands and feet and other regions.

The patient was a boy, aged 6 months, strong and fat, nursed by a healthy mother.

First day: On December 14 a dark, brawny swelling appeared, first in the left foot and then in the right foot. The child seemed ill and cried from pain in his feet. A few hours later a dark red edema involved the scrotum, and an erythema developed on the thighs and buttocks. The baby was given two doses of castor oil, 15 c.c. each, also an enema which caused a normal stool.

Second day: In addition to the edema of the feet and genitals both eyes were closed by an effusion into the lids. The child was in continual misery from the tender ankles and refused to nurse. Fifteen c.c. of castor oil produced three light-colored stools containing mucus and a minute reddish flake, possibly blood.

Third day: Rectal temperature was 100.5; abdomen, heart and lungs normal. The puffiness in the eyelids had lessened. Both ears were swollen with a dark red erythema. There was an ecchymosis the size of a half dollar in each cheek. The scrotum was almost of a nomal size and color. On the back, buttocks and posterior portion of the thigh were numerous dark infiltrated hemorrhagic areas the size of a quarter of a dollar. Both legs were thickly sprinkled with large red papules about 3 mm. in diameter; these evidently itched. Both feet and ankles were greatly swollen and very painful. Here the skin was of a normal color. No abdominal pain or tenderness could be elicited. The urine was scanty and could not be procured.

Fourth day: The baby refused the breast and was in great distress, unless quieted with heroin. The edema in the eyelids and ears was hardly noticeable. As a result of a pin-scratch a broad, dark ecchymosis 7.5 cm. by 0.5 cm. had appeared on the anterior surface of the right thigh. The purpura of the cheeks, back, buttocks and thighs was unchanged. More papules had developed on the legs. Feet and ankles showed no change. Both hands had commenced to swell, the right first.

Fifth day: Baby was asleep from heroin. The most prominent symptom was an enormous swelling of both hands and wrists which had increased so rapidly that the wristbands of the sleeves had to be cut off, leaving a livid constriction in the flesh. All joints in the fingers, hands and wrists were freely movable, but manipulation seemed very distressing. The swelling of the right hand was hard and dark; the color did not change on pressure. In the left hand the edema was equally firm but of a lighter red, which disappeared on pressure. Both legs were covered with urticarial wheals, some of which quickly became hemorrhagic. Mixed with the wheals, but fewer in number, were small petechiae.

Seventh day: The brawny swelling of the hands lasted two days and disappeared. There was no pain in moving either hands or feet. The purpura of the cheeks, back and buttocks was fading; there were new hemorrhagic papules on the legs. The baby was obstinately constipated, probably from opium. It would nurse only after the bowels had moved: there were four laxative stools, large and foul-smelling: there was no blood in them.

Tenth day: Baby very comfortable; sleeping and nursing well: defecation and urination in order. The only relics of the illness were faint stains on the site of the old hemorrhages and a fine papular skin infiltration on the legs.

The child's general condition has remained good, and there has been no recurrence of the skin lesions.

This illness ran its course without fever; no urinary or blood examination could be made. It is practically certain that no serious hemorrhagic nephritis was present as the diapers were not stained by the urine.

SUMMARY

The patient, a fat baby thriving on its mother's milk, was suddenly attacked by purpura, urticaria and localized edema, lasting about ten days. There were only systemic symptoms from the result of pain. At first the bowels were obstinately constipated, possibly from an edema of the intestinal walls sufficient to inhibit peristalsis, but not of enough intensity to cause colic or hemorrhages as is observed in Henoch's purpura.

The skin lesions were (1) an angioneurotic edema of the scrotum, both ears, eyelids, hands and feet; these regions were also discolored by a hyperemia which in the right hand became a brawny hemorrhagic infiltration; (2) numerous papules on the legs; (3) subcutaneous hemorrhages in the cheek, back, buttocks and thighs; (4) the tendency to capillary oozing in the skin, which was so great that a slight pin-scratch caused a long ecchymosis.

The joint symptoms should not be dignified by the title of arthritis; there was a rapid serous effusion into the skin, subcutaneous tissues and peri-articular and articular surfaces of the hands and feet.

The swelling of the feet came first, lasting six days. On the fourth day of the illness both hands were involved. Here the edema remained for three days and was almost hemorrhagic in type. The scrotum, ears, and eyelids were the seat of a transitory edema. Purpura appeared in the face, back and thighs. An urticaria covered both legs.

It should be noted that except in the genitals the skin and joint lesions were symmetrical. All of the symptoms probably belonged to the erythematous group described by Osler, a hemorrhagic type of an exudative diathesis; namely, a vascular dilatation and exudation due

to disturbance of vascular tonus producing hyperemia and serous and hemorrhagic effusions.

In a general angioneurotic disturbance there is an abnormal tendency of the skin, subcutaneous, mucous and articular tissue to react to varied systemic irritants. This toxic influence plays over the peripheral surfaces, producing in some regions localized edemas, on others, urticaria and hemorrhages.

I do not consider the various types of purpura, namely, purpuric arthritis and Henoch's purpura, as distinct pathologic entities. In one region the same toxin may produce an ecchymosis, in another colic and gastro-intestinal hemorrhage, in a third a swollen joint.

The case is reported in full detail not because it is unique, but for the reason that it is a clear-cut example of a purpura and angioneurotic arthritic edema, developing in a young, healthy baby. It is also true that such symptoms might excite unnecessary alarm and false conclusions, were not the short, benign course of the malady well known.

Numerous medical treatises, of which the best is by Pratt, in Osler's Modern Medicine, describe purpura and allied conditions and give illustrative cases, all of which show individuality, and none of which are precisely similar in distribution or character of lesion.

The usual nomenclature and classification of the disease is faulty and leads the enquirer into dire confusion. Nothing definite is known of the etiology. Some authorities claim bacterial infection; others ascribe the symptoms to systemic intoxications of undiscovered origin. Both causes may undoubtedly produce the same lesion. The purpura of a drug rash or scurvy may resemble those of measles or small-pox.

Why a healthy, breast-fed baby should develop purpura, urticaria and swollen joints and recover so quickly, I am unable to explain. It had no fever or digestive disturbance and the function of the kidneys was not disturbed. These facts are against the theory of infection or intoxication.

In this connection a short allusion may be made to Henoch's purpura, in which the purpura is associated with gastro-intestinal crises, acute abdominal pain, vomiting of blood and intestinal hemorrhages. There may be also abdominal tenderness and such obstinate constipation that an intestinal obstruction is suspected, or in a baby the colic, vomiting and bloody stools may simulate the clinical picture of an intussusception.

With these symptoms the experienced clinician might consider operative treatment, but he should also recall the visceral symptoms of the exudative diathesis and look for ecchymosis and localized edemas and a hemorrhagic nephritis. The intestinal symptoms may be caused by an edema of the gastro-enteric mucosa.

Henoch's purpura has a certain surgical importance, for several patients have been operated on for intestinal obstruction and the procedure has done the patient little good. The diagnosis is sometimes made easier by a history of previous attacks, for the condition often recurs. If Henoch's purpura is correctly diagnosed and the patient left alone a prompt recovery is the rule.

ILLUSTRATIVE PERSONAL CASE OF HENOCH'S PURPURA

A girl 2 years old was attacked with an urticarial rash on the flexor surfaces of the thighs. The urticaria was quickly followed by large ecchymoses mixed with petechiae appearing on the chest, abdomen and back.

The purpura faded and was succeeded by a livid swelling of both ears and the right eyelid. About the eighth day of the illness the child commenced to vomit blood and pass two or three bloody mucous stools a day. The gastro-enteric symptoms continued three or four days and ceased abruptly.

During the illness the child was apathetic and somnolent; there was no fever, hematuria or abdominal tenderness.

The child made a complete recovery.

This case differed from Henoch's description, there being no abdominal pain. It is evident that a large number of cases of purpura will show a wide variation in symptoms.

476 Franklin Street.

OTITIS MEDIA; PNEUMONIA; PYELOCYSTITIS; MASTOID DISEASE; FEVER FOR NINE MONTHS, IN AN INFANT AGED SIX TO FOURTEEN MONTHS; FAILURE OF VACCINE; CURE, APPARENTLY, FROM ROENTGEN RAYS

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Baby M., a girl, was born of a healthy father and a mother who was actively tuberculous, both at the time of conception and when her baby was born. The infant was artificially fed from the beginning of its second month, but with indifferent success, for at the age of 6 months it weighed but 12 pounds. This failure in growth seemed to be due to deficient assimilative powers, since the mother insisted that there had never been any evidence of indigestion, and the food given appeared to be of a character quite sufficient for the infant's nutritional requirements.

At 6 months of age, early in April, 1911, the patient caught cold; she had fever, followed by rhinitis and cough. An influenzal "cold" was prevalent at the time and the patient's attack was possibly of this character. A subacute bronchitis soon developed and persisted for two weeks, when high fever (104-105 F.), with pronounced nervous symptoms, ushered in what proved to be an otitis media. The drum-head spontaneously ruptured in three days, with marked amelioration of the general and nervous symptoms.

As is not infrequently observed, the fever did not disappear with the appearance of the aural discharge, but continued in an irregular way, usually running for three or four days between 98.5 and 99.5 or 100.5 F., then rising suddenly to 103, 104 or 105 F., remaining at this point from two to three days, and then falling again to its former level. This peculiar temperature range, with its frequent sudden exacerbations, except during the prevalence of the numerous complicating affections from which the infant suffered, persisted throughout the entire nine months of the illness. The aural discharge also continued during this period; but it did not diminish during the febrile exacerbations, nor increase when the fever was less. There seemed, indeed, to be no connection between the two phenomena.

Local treatment was carried out along accepted lines, and was under the supervision of Dr. O. D. Stickney of Atlantic City, but it had no effect in checking the discharge.

With the onset of the otitis the bronchitis cleared up, but on May 15, 1911, a sudden increase of temperature, rapid breathing and other signs of acute bronchopneumonia manifested themselves. Temperature, 102-104 F.: respirations, 60; pulse, 150; leukocytes, 26,000. The pneumonia involved small areas in both right and left lungs and ran a course of about three weeks, after which the child's temperature continued to pursue the irregular movement described above.

On June 15, 1911, the temperature became continuous again, fluctuating between 101 and 103 F. With this there was increased urination and pain. Examination of the urine gave the following: specific gravity, 1.012; acid; distinct ring of albumin; no sugar; no indican; no casts; a large number of pus-cells; a few blood-cells. This attack of pyelocystitis was treated with urotropin and citrate of potash (1 grain of one and 5 grains of the other, every three hours), and subsided by July 6; that is, the urine became clear and the temperature resumed its irregular course.

On Aug. 1, 1911, the temperature again became continuous and the right mastoid began to swell. Fluctuation was soon apparent; and on August 7 a mastoid operation was performed by Dr. Stickney, a considerable quantity of pus being evacuated. By the middle of September the wound from this operation had healed completely. The slight purulent oral discharge and the fluctuating temperature continued, however, as before.

The exacerbations of temperature occurring, as they did, every fourth or fifth day, and with no apparent relation to the ear discharge, suggested the possibility of malarial infection; but several examinations failed to disclose malarial organisms in the blood, nor did examination of the blood itself throw any light on this point, namely, the cause of the persistent temperature. The following is an average of several blood-counts: leukocytes, 15,000; erythrocytes, 4,000,000; hemoglobin, 65 per cent. Differential count: polymorphonuclears, 45 per cent.; small mononuclears, 45 per cent.; large mononuclears, 8 per cent.; eosinophils, 2 per cent.; no myelocytes nor mast cells.

Because of the mother's active tuberculosis (she had the entire care of the infant and expectorated most freely), the question of tuberculosis

in the patient was met by three von Pirquet tests: one in July, a second on September 10 and a third on Oct. 25, 1911, but no reaction was obtained in any instance. A latent emphysema was also considered, in view of the previous pneumonia, as a cause of the prolonged febrile attacks. Punctures of the pleura, however, twice made (June 25 and June 30), were fruitless.

In November, 1911, there was a recurrence of the pyelocystitis. This attack was more pronounced than the first, and ran a course of about two weeks, when the temperature, which had been running between 102 and 103 F., again resumed its irregular course. The sediment contained numerous pus-cells and albumin was abundant. Six days later a specimen was submitted to Dr. D. H. Bergey of Philadelphia, who reported that the sediment, which was very abundant, contained no pus-cells, no tubercle bacilli, no casts and no epithelium; and that the culture revealed *Streptococcus fecalis*, *Sarcina alba* and *Bacillus coli*, the latter probably being the etiological factor in the pathologic condition. Dr. Bergey saw no reason why pus formation should not cease, as it apparently had, between the first and second examination of the urine. It is not likely that the sarcina had any pathologic significance.

An attempt was made, about November 20, to influence the aural discharge and accompanying fever by the administration of vaccine. Dr. Robert Ivy of Philadelphia isolated from the aural discharge the *Staphylococcus aureus* in pure culture. From this a vaccine was prepared; and eight injections, beginning with 50,000 and increasing, at four-day intervals, up to 2,000,000, were given, without the slightest influence, either on the ear-discharge or on the irregular fever.

Finally, on Jan. 1, 1912, at the earnest solicitation of the parents (who had become possessed with the idea that the Roentgen ray might reveal some other cause than the ear for the infant's prolonged illness, but, of course, with no therapeutic purpose in view), I requested Dr. W. H. Schmidt of Atlantic City to expose the infant to the Roentgen rays. This he did on Jan. 2, 1912, two exposures of ten seconds each being made. The plates disclosed nothing of note, but the temperature, which for several days before the use of the rays had been in the neighborhood of 104 F., fell at once to normal, with a complete cessation of the nine-months' aural discharge. From this time to the present writing, a period of two years, there has been no recurrence of either of these symptoms, except some elevations of temperature from several

incidental affections common to childhood. The application of the Roentgen rays had apparently put an end to the infant's prolonged illness.

That the nutrition of the child suffered from the prolonged fever is readily conceivable. The weight fluctuated considerably. At the age of 6 months the weight was 12 pounds: on Jan. 1, 1912, it was 12¾, a net gain of three-quarters of a pound in nine months.

COMMENT

This case is placed on record for several reasons: first, because of the series of acute and grave affections from which the infant suffered and yet recovered; second, because of the long duration of the fever, although temperature courses, often with fever more continuous than in this case, are not uncommon, and have frequently been recorded, notably, in instances of ulcerative endocarditis. By a process of exclusion, there seems to be little doubt that in this patient the fever was due to the prolonged chronic otitis. The periodical nature of the fever is noteworthy; every three or four days it would rise quickly to 103, 104 or 105 F., remain high for a day or two, and then fall to just a little above normal. It is also of interest that these fluctuations in the temperature apparently bore no relation to the character or the amount of the discharge from the ear. Finally, this clinical history is recorded because of the apparent influence of the Roentgen ray in putting a final stop to the fever and aural discharge.

Anxious to elicit the opinion of others more experienced in these matters than myself, I sought that of Dr. B. Alexander Randall, professor of Otology in the University of Pennsylvania, and that of Dr. George E. Pfahler, Professor of Roentgenology in the Medico-Chirurgical College of Philadelphia. The former replied: "Hundreds of cases of aural perforation are submitted to the Roentgen ray in studying mastoid conditions, and no case has been benefited thereby. The counterirritation, as of a slight burn, might theoretically aid; but I believe so little in anything of the sort that did I not believe it mere coincidence I should ascribe the benefit to the powerful trophic influence of the Roentgen rays." Dr. Pfahler's reply was: "I have not seen any such results from any single exposure to the rays, though if this patient had a series of exposures to the Roentgen rays, it would not be surprising, for I have seen obstinate infections of the maxillary sinus, which had resisted operation and other treatment, respond quickly to the Roentgen ray."

That the Roentgen ray has a powerful trophic and bactericidal influence is well shown by some cases of obstinate ringworm of the scalp presented recently to the Philadelphia Pediatric Society by Dr. F. Crozer Knowles. These cases had resisted, over a long period, every known method of treatment, but were completely cured by a single exposure to the Roentgen ray. Notwithstanding this, I am of the opinion that the case of apparent cure of prolonged otitis media chronica with fever by the Roentgen ray, herein reported, should be regarded as an interesting observation and not as a conclusion.

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American Pediatric Society
Transactions